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Systematic review

Effectiveness of conservative non-pharmacological interventions in people with muscular dystrophies: a systematic review and meta-analysis

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ABSTRACT

Introduction Management of muscular dystrophies (MD) relies on conservative non-pharmacological treatments, but evidence of their effectiveness is limited and inconclusive.

Objective To investigate the effectiveness of conservative non-pharmacological interventions for MD physical management.

Methods This systematic review and meta-analysis followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and searched Medline, CINHAL, Embase, AMED and Cochrane Central Register of Controlled Trial (inception to August 2022). Effect size (ES) and 95% Confidence Interval (CI) quantified treatment effect.

Results Of 31,285 identified articles, 39 studies (957 participants), mostly at high risk of bias, were included. For children with Duchenne muscular dystrophy (DMD), trunk-oriented strength exercises and usual care were more effective than usual care alone in improving distal upper-limb function, sitting and dynamic reaching balance (ES range: 0.87 to 2.29). For adults with Facioscapulohumeral dystrophy (FSHD), vibratory proprioceptive assistance and neuromuscular electrical stimulation respectively improved maximum voluntary isometric contraction and reduced pain intensity (ES range: 1.58 to 2.33). For adults with FSHD, Limb-girdle muscular dystrophy (LGMD) and Becker muscular dystrophy (BMD), strength-training improved dynamic balance (sit-to-stand ability) and self-perceived physical condition (ES range: 0.83 to 1.00). A multicomponent programme improved perceived exertion rate and gait in adults with Myotonic dystrophy type 1 (DM1) (ES range: 0.92 to 3.83).

Conclusions Low-quality evidence suggests that strength training, with or without other exercise interventions, may improve perceived exertion, distal upper limb function, static and dynamic balance, gait and well-being in MD. Although more robust and larger studies are needed, current evidence supports the inclusion of strength training in MD treatment, as it was found to be safe.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The management of muscular dystrophies (MD) primarily rely on conservative non-pharmacological interventions, including strength and aerobic training, orthotic devices, aids and assistive technologies, as there is currently no cure to halt MD progression. However, evidence supporting the effectiveness of these conservative non-pharmacological interventions is limited and inconclusive. This systematic review and meta-analysis was undertaken to better understand the effectiveness of these interventions on the physical manifestations of MD, including non-randomised and uncontrolled studies, which constitute the predominant body of literature in this field but have been omitted from prior evidence syntheses.

WHAT THIS STUDY ADDS

⇒ This study revealed that strength training, alone or combined with other exercise interventions, may improve perceived exertion, distal upper limb function, static and dynamic balance, gait and well-being in individuals with MD despite no significant structural changes.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ These positive findings, although based on low-quality evidence, have possible clinical implications as they contradict historical apprehensions about the potential harm associated with exercise interventions in MD. Therefore, our findings suggest that strength training, whether as a standalone intervention or within a multicomponent programme, should be considered a fundamental component in the treatment of MD.

INTRODUCTION

Muscular dystrophies (MD) have an estimated prevalence ranging between 19.8 and 25.1/100,000.[1] MD are a clinically and genetically heterogenous group of muscle disorders, sharing common dystrophic pathological features, such as variable muscle fibre size and necrosis, resulting in fatty or fibrotic tissue replacement and progressive muscle wasting and weakness.[2 3] MD are commonly progressive and disabling over time, despite differences in their rate and pattern of progression with variation in how the limb, axial, facial, ocular and pharyngeal muscles are affected.[4] Specific MD forms can also affect respiratory and cardiac muscles.[5] These result

in people with MD experiencing reduced motor functioning, social participation and quality of life.[6]

There is no cure to halt MD progression despite therapeutic advances in the most common forms of MD in the last two decades.[7] Individuals with MD rely on surgical and non-pharmacological treatments, including strength and aerobic training, orthotic devices, aids and assistive technologies.[8] Although conservative non-pharmacological interventions are essential part of the MD management, evidence supporting their effectiveness is limited and inconclusive.[9 10] Despite some common impairments between MD, there may be pathobiological mechanisms unique to each MD subtype.[2] Therefore, the effectiveness of an intervention may not be transferrable between MD subtypes as the therapeutic mechanism may not be optimal. Conservative interventions require appropriately tailoring to the symptoms and abilities of individuals with MD in order to be beneficial and not harmful. Inappropriate intervention type and dose can lead to detrimental effects, such as overwork weakness, fatigue, discomfort and pain.[11]

A wider understanding of the effects of conservative non-pharmacological interventions in people with MD is needed. This systematic review and meta-analysis aimed to determine the effectiveness of existing interventions, focusing only on those targeting physical impairments, excluding respiratory management.

METHODS

This systematic review with meta-analysis was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[12] The review protocol was not registered.

Literature search strategy

Medline, CINHAL, Embase, AMED and the Cochrane Central Register of Controlled Trial were systematically searched from inception to 22 August 2022. The search was supplemented by searching the reference lists of relevant articles and reviews. Search strategies available in online supplemental file 1.

Study selection process

Records were exported into a reference management tool (Mendeley, Elsevier B.V.) and duplicates were removed. Any remaining duplicates were removed manually. One reviewer (EL) screened the records, with verification by two other researchers (FP, AP). Records were initially screened by title and abstract, followed by full-text analysis of relevant studies.

Inclusion and exclusion criteria

Studies were included if (1) involved humans with MD or neuromuscular diseases (NMD), data were separate for MD, (2) investigated conservative non-pharmacological interventions, alone or combined with other conservative non-pharmacological therapies, (3) had ≥5 participants per group, (4) had full texts available and (5) published in peer-reviewed journals.

Studies were excluded if (1) included pharmacological or surgical treatments, (2) unavailable data, (3) assessed conservative non-pharmacological interventions for respiratory and cognitive manifestations and (4) solely focused on non-pertinent outcomes (e.g. respiratory and cognitive outcomes).

Authors were contacted for missing data. If no response or unextractable data, studies were excluded.

Data extraction

One reviewer (EL) extracted data (online supplemental file 2). Non-English articles were translated by the research team where appropriate.

Quality assessment

Two reviewers (EL, FP) independently assessed the methodological quality of the included Randomised Controlled Trials (RCTs) using the Cochrane 'Risk of Bias' Tool.[13] Studies with research designs other than RCT are by nature at high risk of bias, and so no formal quality appraisal was undertaken. Uncertainties and disagreements between reviewers were resolved in team discussions.

Statistical analysis

ES was calculated using Cohen's d formula.[14] As most available evidence comes from non-randomised, uncontrolled studies, ES calculation was performed in all studies, including quasi-controlled studies, although they were a priori considered at high risk of bias. Further information about ES calculation is provided in online supplemental file 3. The absolute magnitude of ES was classified as small (0.20–0.49), medium (0.50–0.79), large (0.80–1.29) and very large (≥1.3).[14] If the 95% Confidence Interval (CI) range of the ES did not include zero, the result was considered statistically significant. Included studies were primarily clustered based on the type of intervention tested (orthotic devices, manual therapy, assistive technologies and exercise interventions), secondly by intervention subtype.

ESs were reported for the intervention types and subtypes, and outcomes were mapped to the International Classification of Functioning, Disability and Health (ICF).[15] Formal heterogeneity assessment was not conducted as statistical heterogeneity was expected due to variability in sample sizes, MD type, conservative non-pharmacological treatment types and outcome measures. Following data extraction, ES data were normalised. Regardless of the direction of change in the outcome, positive signs were used to represent positive changes from baseline, while negative signs were used to indicate negative changes with scores worsening compared with baseline.

RESULTS

Study identification

The search identified 31,285 articles, reduced to 17,014 after removing duplicates. After screening the titles and abstracts, 221 were deemed suitable for full-text review; 38 of them fulfilled the eligibility criteria and were included. A further manual search identified 33 additional articles; of them, 29 progressed to full-text review and once reviewed, one was considered eligible for this study. Finally, a total of 39 articles were included. Figure 1 describes the study selection process.

Study characteristics

Included studies comprised 15 RCTs and 21 quasi-controlled studies, predominantly before–after designs without a control group (18/21). Most studies were published in the last decade (74%, 29/39), mainly from Europe (69%, 27/39). Included studies involved a total of 957 participants (range: 6–255). DMD (n=13 studies), DM1 (n=11 studies) and FSHD (n=8 studies) were the most explored MD forms (online supplemental file 4). Most cohorts consisted of adults only (67%, 26/39). All except one[16] of the paediatric studies involved children with DMD. Most studies had a male predominance (male:female ratio=2:1). Most studies included ambulatory participants, but mobility

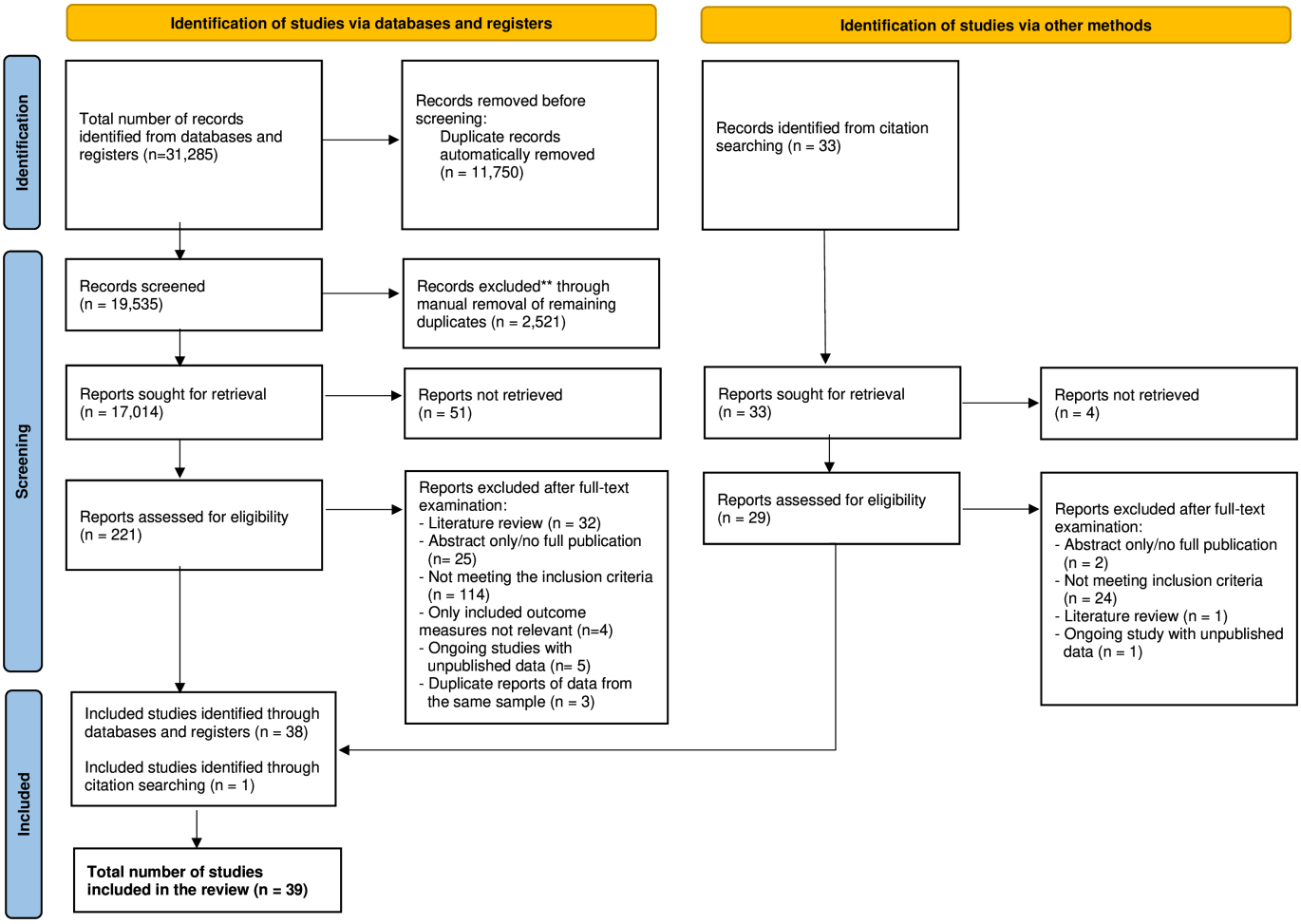


Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart of the study selection process. CBT, Cognitive Behavioural Therapy.

levels were variable, ranging from independently mobile,[17–22] mobile with or without assistive aids[23–28] to wheelchair dependent.[29 30] Similarly, upper-limb abilities varied from grade one, where individuals could lift their arms above their head, to grade four on the Brooke Upper-Extremity Scale,[31] where they could raise hands to mouth, but they could not bring a glass of water to their mouth. Further study characteristics supplied in online supplemental file 5.

Risk of bias

Figure 2 shows the risk of bias for the included RCTs. Twelve of the 15 RCTs[17 23 28–30 32–38] were considered at high risk of bias and 'some concerns' arose for three RCTs.[20 24 39] All studies confirmed randomisation, but four studies[29 36–38] did not report concealed allocation information. Baseline differences between study groups were observed in three studies.[17 24 35] Patient participants were not blinded in any of the RCTs, but six studies[20 24 30 35 38 39] reported blinding of the assessors. Nevertheless, almost 50% of studies (7/15)[17 28 29 32–34 36] were considered at high risk of bias in outcome measurement as they adopted assessor dependent outcome measures. Eight studies[3 17 23 28–30 35 38] had attrition bias due to missing outcome data or study participants' drop out[17 23 28–30 35 38 39]; however, most studies adopted an appropriate analysis to explore the effect of assignment to intervention. Only one study documented protocol deviations.[23] Thirteen studies did not provide a statistical analysis plan, causing selection bias risk.

Conservative non-pharmacological interventions

Conservative non-pharmacological interventions were classified into four types: orthotic devices, manual therapy, assistive technologies and exercise interventions. An overview of the intervention types, subtypes and MD subgroups studied is presented in figure 3. Further details are available in online supplemental files 6 and 7.

Of the 39 included studies, seven [19–21 25 34 36 40] (three RCTs[20 34 36] and four non-RCTs[19 21 25 40]) observed a statistically significant treatment effect in one or more of their outcomes, with a total of nine outcome measures being improved. Significant improvements were mainly seen in functional outcomes (5/9),[21 25 32 34] mostly pertaining balance abilities (3/9).[25 34] Most outcomes (7/9) improved following supervised exercise interventions.[21 25 34 36 40] Seven of the nine outcomes, which included perceived exertion, distal upper-limb function, gait, static and dynamic balance and self-perceived physical condition, improved following training programmes including strength exercises alone[25 40] or combined with other exercise modalities (e.g. aerobic and balance training).[20 21 34] Non-exercise interventions significantly improved only a small number of outcome measures (2/9).[19 41] The largest significant ES was observed in Borg Rating of Perceived Exertion (RPE) (ES: 3.83 (95% CI: 2.86 to 4.79)),[20] and the smallest significant ES was observed in dynamic balance (sit-to-stand ability) following strength training (ES: 0.83 (95% CI: 0.08 to 1.58)).[25] There were a large number

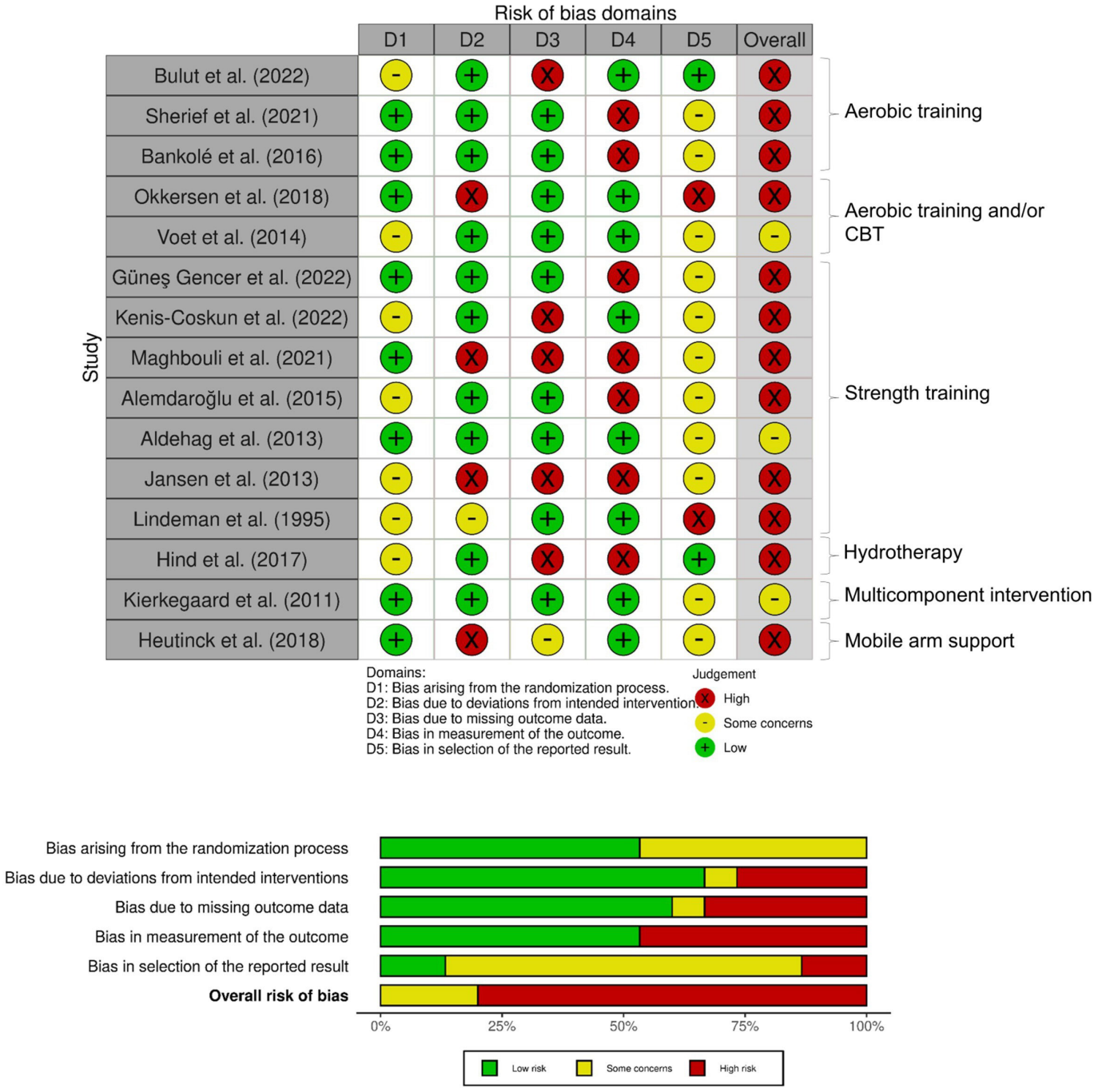


Figure 2 Risk of bias summary for randomised controlled trials only.

of outcomes, and many studies reported non-significant treatment effects. Therefore, the following paragraphs will provide a narrative overview only of those intervention subtypes with fewer studies. For intervention subtypes with a large number of studies, only the largest and significant ESs will be reported. Results for all interventions are displayed in figure 4 with further details presented in online supplemental file 8. A graphical representation of statistically significant ESs across all included studies is presented in figure 5.

Orthotic devices

Three studies[42–44] (two[43 44] before–after studies without control group and one[42] case series study) involving a total of 33 participants investigated orthotic devices (serial casting[42] and AFO/FO[43] in children with DMD, and KAFO in adults with FSHD[44]). None of the improvements recorded were statistically significant; positive ESs ranged from 0.09 (VAS pain after AFO/FO[43]) to 2.73 (ankle dorsiflexion passive range of motion after serial casting[42]).

Manual therapy

One crossover study[18] investigated calf massage in children with DMD. Small to moderate ESs observed in lower-limb muscles length and gait were not statistically significant. ESs ranged from −0.52 in knee extension range of motion after calf massage to 0.62 in ankle dorsiflexion range of motion with knee extended.

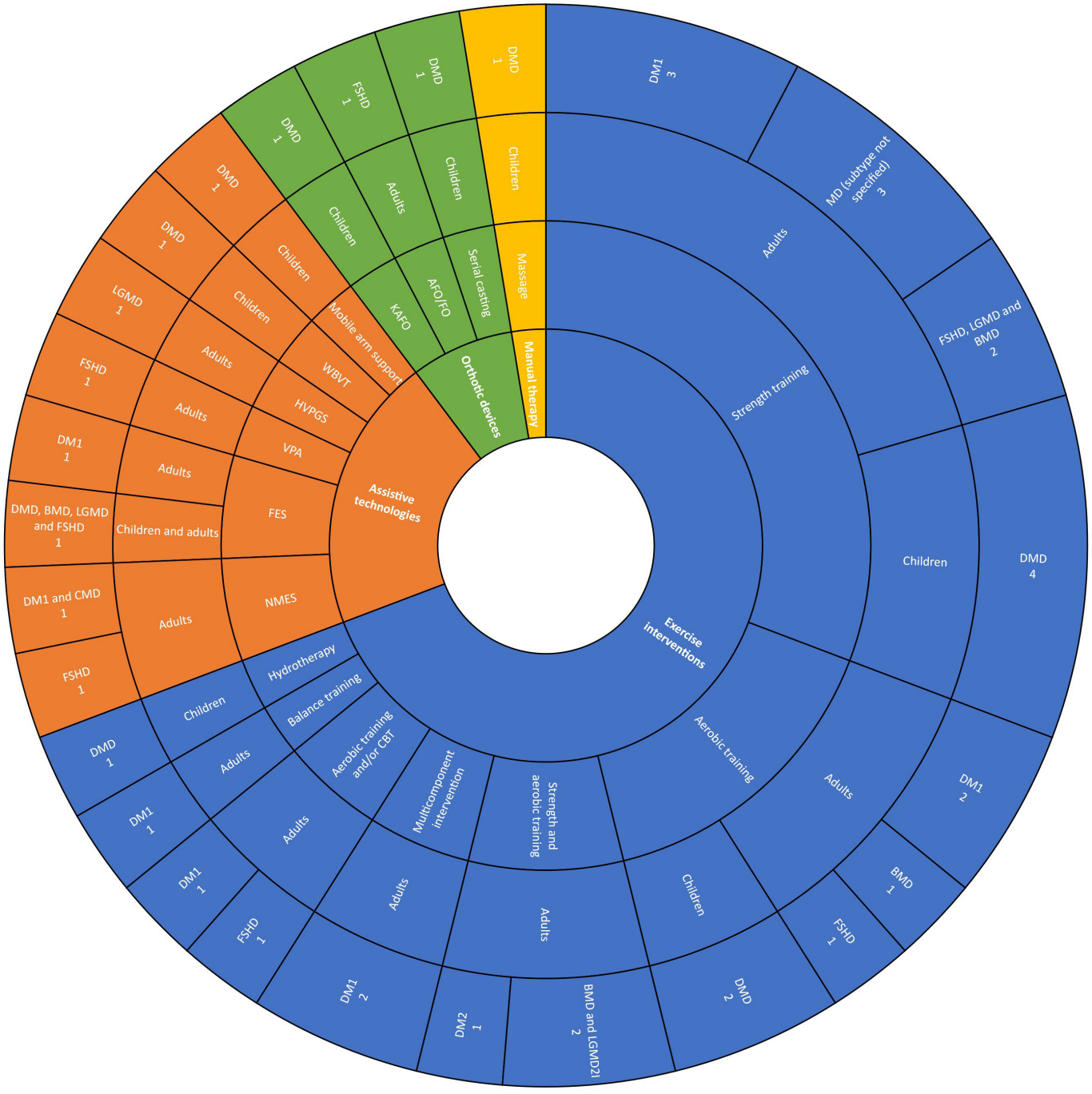


Figure 3 Sunburst chart of the characteristics of the included studies. AFO, Ankle Foot Orthosis; BMD, Becker Muscular Dystrophy; CBT, Cognitive Behavioural Therapy; CMD, Congenital Myotonic Dystrophy; DM1, Myotonic Dystrophy type 1; DM2, Myotonic Dystrophy type 2; DMD, Duchenne Muscular Dystrophy; FES, Functional Electrical Stimulation; FO; Foot Orthosis; FSHD, Facioscapulohumeral Dystrophy; HVPGS, High Voltage Pulsed Galvanic Stimulation; KAFO, Knee Ankle Foot Orthosis; LGMD, Limb Girdle Muscular Dystrophy; LGMD2I, Limb Girdle Muscular Dystrophy type 2I; MD, Muscular Dystrophy; NMES, Neuromuscular Electrical Stimulation; VPA, Vibratory Proprioceptive Assistance; WBVT, Whole-Body Vibration Training.

Assistive technologies

Nine studies,[16 19 22 30 41 45–47] of which all except one[30] had before–after study design, explored assistive technologies interventions. Sample sizes ranged from six to 24 participants, totaling 97 participants, with study durations of two to 20 weeks. Overall evidence quality was low, as eight studies were at high risk of bias due to research designs. The only RCT[30] had methodological limitations due to deviations from the intended intervention.

Gravity-compensated training with a suspension mobile arm support,[30] whole-body vibration training,[45] high volt pulsed galvanic stimulator[22] and functional electrical stimulation[16 47] did not produce statistically significant treatment effects. In contrast, NMES significantly reduced pain in nine adults with FSHD (ES: 1.58 (95% CI: 0.61 to 2.55)).[19] Furthermore, vibratory proprioceptive assistance (VPA) (4-week training, 8 total sessions at 80 Hz) significantly improved shoulder abduction muscle strength in nine adults with FSHD (ES: 2.33, 95% CI: 1.32

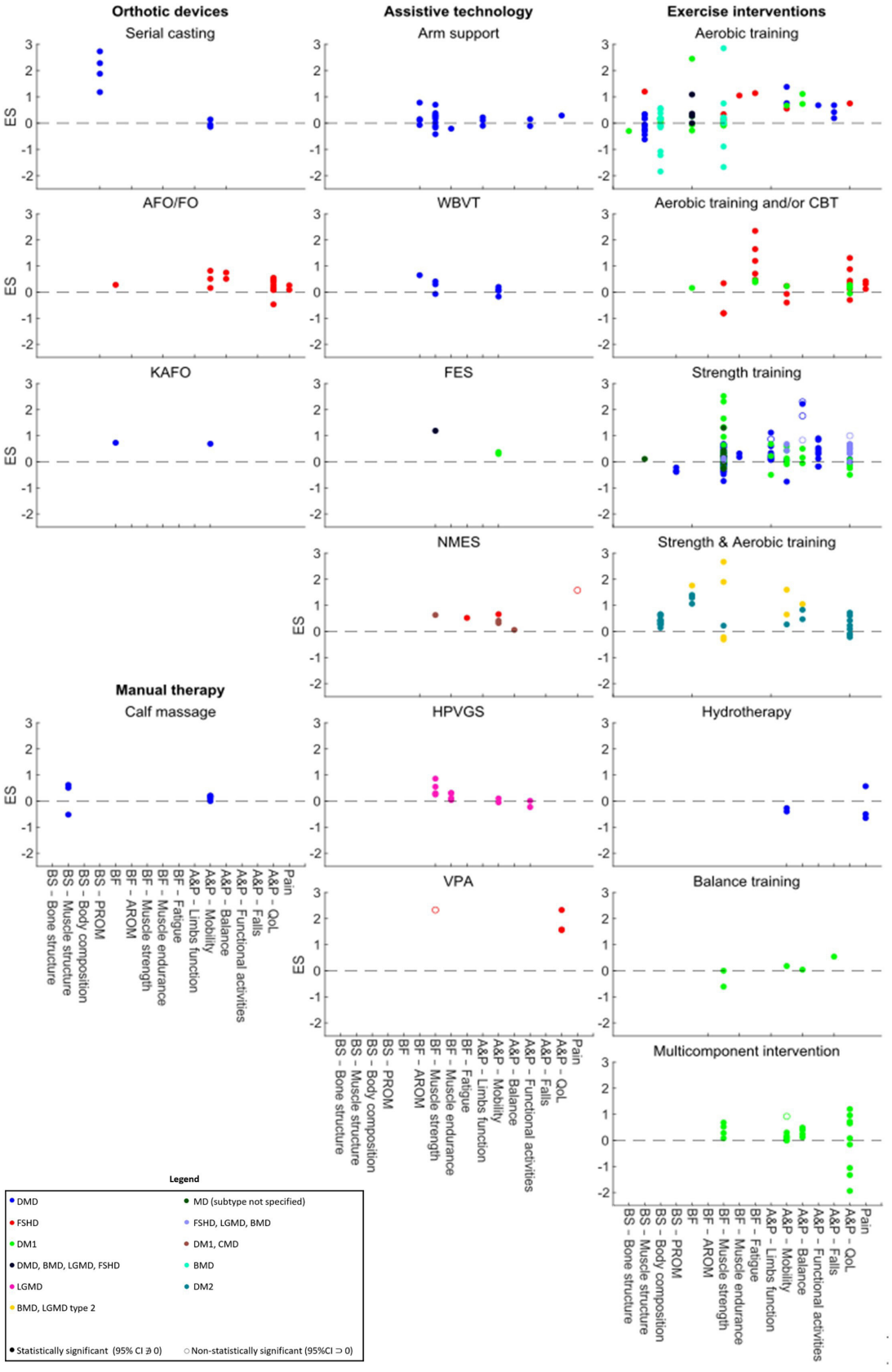
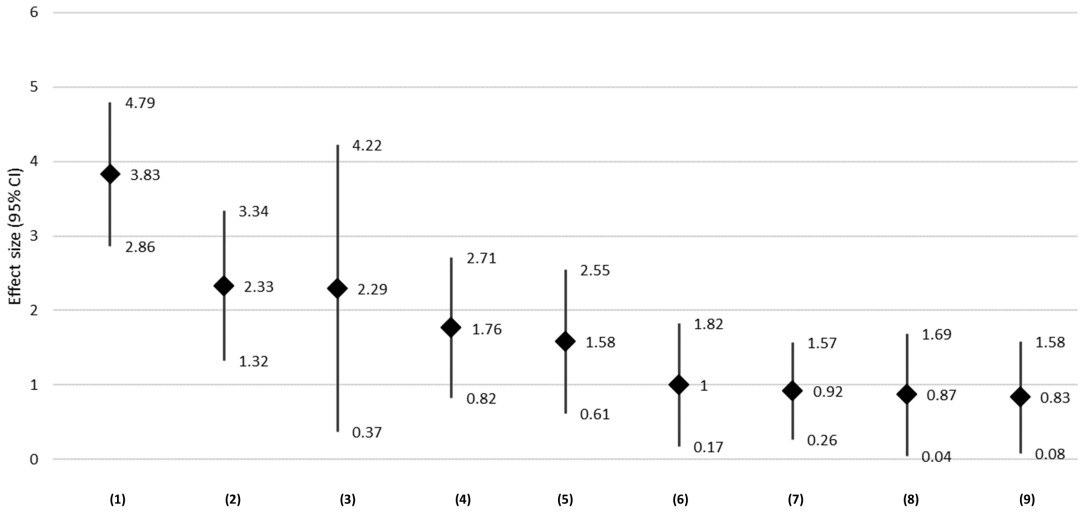


Figure 4 Scatter plots of the effect sizes of the included conservative non-pharmacological interventions. A&P, Activity and Participation; AFO/FO, Ankle Foot Orthosis/Foot Orthosis; AROM, Active Range of Motion; BF, Body Function; BMD, Becker Muscular Dystrophy; BS, Body Structure; CBT, Cognitive Behavioural Therapy; CMD, Congenital Muscular Dystrophy; DM1, Myotonic Dystrophy type 1; DM2, Myotonic Dystrophy type 2; DMD, Duchenne Muscular Dystrophy; ES, Effect Size; FES, Functional Electrical Stimulation; FSHD, Facioscapulohumeral Muscular Dystrophy; HPVGS, High Volt Pulsed Galvanic Stimulator; KAFO, Knee Ankle Foot Orthosis; LGMD, Limb-Girdle Muscular Dystrophy; MD, Muscular Dystrophy; NMES, Neuromuscular Electrical Stimulation; PROM, Passive Range Of Motion; QoL, Quality of Life; VPA, Vibratory Proprioceptive Assistance; WBVT, Whole-Body Vibration Training.



ID	Study authors	Intervention	Outcome	ES	95% CI
1	Kierkegaard et al. (2011)	Multicomponent program*	Perceived Exertion (Borg RPE)	3.83	(2.86; 4.79)
2	Ribot-Ciscar et al. (2015)	VPA	Shoulder abduction MVIC	2.33	(1.32; 3.34)
3	Güneş Gencer et al. (2022)	Trunk-oriented strength training plus usual care vs usual care alone	Dynamic reaching balance (TCMS)	2.29	(0.37; 4.22)
4	Güneş Gencer et al. (2022)	Trunk-oriented strength training plus usual care vs usual care alone	Sitting balance (TCMS)	1.76	(0.82; 2.71)
5	Colson et al. (2010)	NMES program	Pain (VAS)	1.58	(0.61; 2.55)
6	O'Dowd et al. (2022)	Strength training	Self-perceived physical condition (PSPP-R)	1	(0.17; 1.82)
7	Missaoui et al. (2010)	Multicomponent program*	Gait speed	0.92	(0.26; 1.57)
8	Güneş Gencer et al. (2022)	Trunk-oriented strength training plus usual care vs usual care alone	PUL distal score	0.87	(0.04; 1.69)
9	Bostock et al. (2019)	Strength training	Dynamic balance (STS)	0.83	(0.08; 1.58)

Figure 5 Forest plot of the significant effect sizes in the included studies. ES, Effect Size; MVIC, Maximum Voluntary Isometric Contraction; NMES, Neuromuscular Electrical Stimulation; PSPP-R, Physical Self-Perception Profile Revised; PUL, Performance of Upper Limb; RPE, Rating of Perceived Exertion; STS, Sit To Stand; TCMS, Trunk Control Measurement Scale; VAS, Visual Analogue Scale; VPA, Vibratory Proprioceptive Assistance.

to 3.34).[41] ESs across studies ranged from −0.42 in shoulder abduction strength after arm support[30] to 2.33 in both shoulder abduction muscle strength and self-rated health state after VPA.[41]

Exercise interventions

A total of 27 studies,[17 20 21 23–29 32–40 48–55] including 14 RCTs,[17 20 23 24 28 29 32–39] 12 before–after studies[25–27 29 40 48–50 52–55] (three with a control group[49 54 55]) and one retrospective study,[21] explored exercise interventions lasting from four weeks to 10 months (807 total participants, range: 6–255). Interventions included strength training or aerobic training, alone or in combination with each other or other conservative treatments like cognitive–behavioural therapy (CBT), balance training and hydrotherapy. Overall evidence quality was low, with 13 studies at high risk of bias due to study design. Fourteen RCTs were at either moderate or high risk of bias, predominantly due to assessor-dependent outcome measures, attrition and inappropriate analysis of intervention assignment.

ESs ranged from −1.94 in the social functioning item of the 36-Item Short Form Survey (SF-36) after a multicomponent intervention[20] to 4.00, observed in lunges performance after an intervention combining aerobic and strength training.[51]

Aerobic training

Six studies[32 33 38 53–55] used aerobic training as an intervention, with five studies[32 38 53–55] using a cycle ergometer, either solely for lower-limb training[32 38 53 54] or compared with a treadmill.[32] One study[37] used a stationary ergocycle for lower-limb training only. Half of the studies were RCTs[32 33 38] and half were before–after studies[53–55] (two had a control group[54 55]). A total of 115 participants underwent aerobic training (range: 11–30 participants), with follow-up periods ranging from 12 weeks to 12 months. Quality of evidence was low due to a high risk of bias resulting from missing outcomes and outcome measurement.

None of the aerobic exercise interventions yielded statistically significant effects in the measured outcomes.

Aerobic training and/or CBT

Two RCTs[23 24] explored aerobic training and CBT, given alone, in combination with each other or in addition to usual care, in 312 adults with FSHD[24] and DM1.[23] Okkersen *et al*[23] found no superiority of CBT and aerobic training combined with usual care over usual care alone (ES range: −0.05 to 0.45). Despite improvements in fatigue (ES range: 0.41 to 2.35) and quality of life (ES range: 0.12 to 1.31), Voet *et al*. [24] showed no statistically significant changes in any outcomes.

Strength training

Twelve studies,[25–29 34–37 39 40 49] predominantly using RCT design (7/12),[28 29 34–37 39] explored strength interventions in 276 participants (range: 9–40 participants). Four[29 34–36] studies involved children with DMD, while the remaining studies[25–28 37 39 40 49] examined adults with DM1, DM2, FSHD, LGMD, BMD and unspecified MD subtypes. The quality of evidence for RCTs ranged from 'some concerns' to 'high' due to moderate risk of selection bias and high risk of bias from missing data and outcome measurement.

Strength training interventions did not yield statistically significant changes in terms of muscle structure,[49] passive range of motion,[29] muscle strength[25–29 35–37 39] and mobility.[25–27 29 35 36] Nevertheless, Güneş-Gencer *et al*[34] found that eight weeks of

trunk-oriented training combined with conventional care was significantly more effective than conventional care alone for improving distal wrist and hand function (PUL distal subscore) (ES: 0.87 (95% CI: 0.04 to 1.69)) in children with DMD.

Balance abilities significantly improved following strength training in two studies.[25 34] Güneş Gencer and Yilmaz[34] observed that eight-week trunk-oriented exercises combined with usual care were more effective than usual care alone in improving static sitting (ES: 1.76 (95% CI: 0.82 to 2.71)) and dynamic reaching balance (ES: 2.29 (95% CI: 0.37 to 4.22)) in children with DMD. Additionally, Bostock *et al*[25] observed that the timed sit to stand test of adults with FSHD, LGMD and BMD significantly improved after a 12-week strength training (ES: 0.83 (95% CI: 0.08 to 1.58)).

In adults with FSHD, LGMD and BMD, the same research group[25] observed a significant improvement in self-perception of physical condition (ES: 1.00 (95% CI: 0.17 to 1.82)).[40] Strength training did not improve any other quality-of-life domains (ES range: −0.50 to 0.67).[29 35 39 40]

Strength and aerobic training

Three before–after studies without control group[50–52] adopted intervention programmes involving strength and aerobic training in a total of 26 adults (range: 8–10 participants) with DM2, BMD and LGMD2I. One study[52] used a four-week programme (two times/week) on a stationary bicycle, while the other two studies,[50 51] from the same research group, used a 10-week programme (three times/week, 40 min/session) on an antigravity treadmill. No statistically significant differences were noted in the outcome measures assessed.

Hydrotherapy

One RCT[17] involving 12 children with DMD found that six-month hydrotherapy combined with land-based exercises had non-significant effects on all outcome measures (ES range: −0.65 to −0.27).

Balance training

One uncontrolled before–after study[48] with 11 adults with DM1 explored a group balance programme (one to three times/week, 60 min/session, for 10 weeks), reporting non-significant treatment effects.

Multicomponent interventions

Two studies,[20 21] one RCT[20] and one retrospective study,[21] used multicomponent rehabilitation programmes, comprising flexibility, aerobic, strength and balance training, for a total of 55 adults with DM1. One study[21] showed significantly greater fast walking speed (ES: 0.92 (95% CI: 0.26 to 1.57)), while the other[31] observed statistically significant changes in the Borg RPE score after training (ES: 3.83 (95% CI: 2.86 to 4.79)).

Adverse events

Over 35% (14/39) of studies reported adverse events, with low frequency among participants. The most reported adverse event was pain (n=33 participants)[24 27 29 30 37 42 45 49] which mostly affected the lower back[24 27 37] and lower limbs.[29 49] Other adverse events were muscle soreness,[17] cramp,[45] fatigue,[53] falls,[17 23] foot fracture,[45] physical discomfort,[49] skin redness[19 42] and skin irritation.[45] Most participants successfully completed programmes with only transient symptoms consistent with the interventions. Okkersen *et al*[23] reported that that 50% of the participants (n=255) experienced adverse events, which were serious in 13% of the cases. However, not all reported adverse events were directly attributed to the exercise interventions (e.g. upper respiratory tract infection and neoplasm). Another three studies[17 29 30] reported adverse events unrelated to the intervention tested. Only one study[27] reported significant long-term adverse events (low back pain) from exercise protocol. Only two patients dropped out due to adverse events (back pain) related to the intervention.[37 49]

DISCUSSION

This systematic review and meta-analysis explored the effectiveness of conservative non-pharmacological interventions for the MD physical management. Although various improvements were observed, most intervention effects were non-significant. Low-quality evidence suggests that exercise interventions incorporating strength training may enhance functional abilities. Specifically, a multicomponent rehabilitation programme, consisting of strength, flexibility and balance training, improved gait speed in adults with DM1.[20] Additionally, adults with FSHD, LGMD and BMD[25] showed enhanced dynamic balance (sit-to-stand ability) after strength exercises. For children with DMD, trunk-oriented strength exercises combined with usual care were more effective than usual care alone to improve distal upper-limb function, static sitting and dynamic reaching balance.[34] Interestingly, these functional improvements occurred without substantial muscle strength changes. Only one study implementing VPA in FSHD[41] found statistically significant muscle strength changes. This may suggest that conservative non-pharmacological interventions, including strength training, may help maintain, rather than improve, muscle strength in MD. However, the strength interventions durations did not exceed six months, making it unclear whether continuous interventions can maintain muscle strength in the long term despite the MD progressive nature. Furthermore, it is important to acknowledge the divergence in muscle strength findings; while some studies reported non-significant improvements, others observed non-significant declines after training. This decline could be attributable to the MD degenerative nature, but the exact cause remains uncertain, as the variability in intervention characteristics (e.g. intensity, duration) and study populations (e.g., disease type and severity) where this was observed makes it difficult to determine the responsible factors.

The positive findings from strength training interventions have possible clinical implications given historical concerns about exercise interventions potentially causing harm in MD.[56] They support the use of strength training, either independently or with complementary exercise interventions, as this approach not only has proven to be safe when carried out using existing parameters and could be cost-effective, but also seem to ensure an efficient training stimulus.[9] Using strength training in multimodal interventions may address multiple impairments simultaneously. While intervention characteristics were variable, the strength training component within interventions that yielded statistically significant differences typically included supervised active or active-assisted strength exercises, using free weights or exercise machines. Exercise sessions generally took place twice a week (ranging from twice a week to daily) for eight weeks, and each session lasted approximately 40–45 min (range: 40 min to two hours); exercises typically consisted of five to 10 repetitions for one to three sets. While available studies suggest the beneficial effects of this dosage, there is not yet sufficient evidence to make recommendations. Notably, supervision may have influenced health behaviour change and the effectiveness

of these interventions, resulting from education, opportunities and capability which facilitate adherence levels.[57] It is important to note that strength interventions improved balance abilities, while balance-specific programmes failed to yield any significant balance changes.[47] This may indicate that (1) strength training, alone or combined with other exercise forms, may be more beneficial than balance-specific exercises alone; (2) strength loss significantly impacts other body structures and activities and (3) some balance assessments (e.g. timed up and go test) may show improvements reflective of muscle strength changes. These observations also suggest that intervention effectiveness assessment through functional outcomes may be more appropriate than relying solely on strength measures, considering that muscle strength improvements may not always occur due to progressive muscle weakness in these conditions.

Most non-exercise interventions (manual therapy, orthotic devices and assistive technologies interventions) did not produce statistically significant treatment effects. This was likely due to study limitations, including small sample sizes, lack of blinding, missing data and dropouts. These limitations were more pronounced in non-exercise interventions due to their smaller scale, potentially explaining their lower frequency of significant results compared with exercise interventions. Non-exercise intervention studies typically involved the smallest sample sizes (range: 9–24 participants), further exacerbated by dropouts observed in a third of the non-exercise intervention studies. Furthermore, most non-exercise interventions were tested within single MD clinical groups, leaving treatment effects variations across MD conditions unexplored. Unlike exercise interventions that often used more structured and supervised regimens, non-exercise interventions were primarily unsupervised, leaving adherence rates uncertain and potentially influencing their effectiveness. Additionally, the assessment of non-exercise interventions focused on a limited number of outcome measures, which may have not captured the full spectrum of potential effects, possibly leading to an underestimation of their impact. Despite most non-exercise interventions lacking statistical significance, it is important to acknowledge that many of them are commonly integrated into the MD clinical management or recommended on an individual basis. In the absence of a robust evidence base, healthcare professionals and clinical services use these interventions as they are deemed to be acceptable, feasible, and beneficial by healthcare providers and people with MD. With no cure available, offering these conservative non-pharmacological interventions addresses symptoms, meets patient expectations, and empowers healthcare professionals to make a positive impact on their patients' lives. For individuals living with MD, receiving these interventions goes beyond merely alleviating physical symptoms; it potentially cultivates hope and fosters resilience, improving their overall experiences of living with MD. In clinical practice, these interventions target impairments affecting fatigue levels, psychological well-being, independence, engagement in social activities and quality of life. However, the perceived benefits of these interventions haven not been substantiated by this systematic review and meta-analysis due to inherent study limitations, rather than the ineffectiveness of the interventions themselves, which may have confounded their true effects, making them appear less impactful than they are in routine clinical practice.

Existing guidelines for conservative non-pharmacological management of MD, as well as other NMD, are limited[56] or neglect conservative non-pharmacological approaches[58] due to the absence of robust evidence supporting their clinical benefits, negatively affecting clinical decision-making.[59] While existing guidelines often overlook these interventions, their role within an evidence-based practice framework, their potential efficacy, their safety and the absence of alternative treatments may justify their clinical use, especially strength training alone or combined with other exercise forms. However, to employ conservative non-pharmacological interventions of which evidence is yet to fully become available, these interventions should align with first principles, be acceptable to patients and healthcare professionals, pose no harm or financial burden, and be continually reviewed for adherence to evidence-based practice. Where the evidence suggests treatment is beneficial (e.g. strength training), we should continue to work towards monitoring risk of harm while also exploring how to optimise the prescriptions to maximise benefits. Furthermore, while this review and meta-analysis did not include studies combining conservative non-pharmacological treatments with pharmacological interventions, preventing a direct comparison of their effectiveness, previous research in MD and NMD suggests that conservative non-pharmacological interventions have comparable, if not superior, effectiveness than pharmacological treatments.[60 61] For instance, very large, although non-significant, ESs (range: 1.46–8.93) strongly favoured conservative interventions over pharmacological treatments in specific outcomes (e.g. Berg balance, grip strength, 2-min walk test, physical functioning, role limitations due to physical health and emotional problems) in the study by Connor *et al*.[60]

Numerous questions regarding the effectiveness of these interventions remain unanswered, specifically about certain outcomes, populations and intervention types. Pain, a common and distressing symptom in MD,[62 63] offers anecdotal indications of potential relief through non-pharmacological interventions such as hydrotherapy. However, the impact of conservative interventions on pain is underexplored, with most studies failing to demonstrate statistically significant improvements. Only a small-scale NMES study in adults with FSHD reported a significant reduction in pain.[19] Furthermore, most studies involved adults only, and all except one[16] of the studies involving children were conducted in DMD. No studies have explored the effectiveness of conservative non-pharmacological interventions in infantile and juvenile cases of MD forms other than DMD. Additionally, there is limited exploration of interventions in the early stages of these conditions. Most studies focused on exercise interventions, leaving the effectiveness of non-exercise interventions unknown. Studies on conservative non-pharmacological interventions in adults with DMD are scarce, and the effectiveness of upper-limb orthoses remain unclear.

Future studies are required to advance current understanding of the effectiveness of conservative non-pharmacological interventions for MD. To overcome existing challenges and conduct studies that genuinely capture the effectiveness of these interventions, several actions are imperative.

Alternative study designs and methods for determining effectiveness of therapy interventions in MD are needed. While RCTs remain the gold standard for assessing intervention effectiveness, the diseases rarity, MD phenotypic heterogeneity, logistical complexities and patients' geographical dispersion often make RCTs challenging. Where existing treatment options are limited or non-existent, people with MD usually prefer access to an active intervention rather than a placebo. Within a research landscape increasingly focused on developing disease-modifying treatments, individuals may find participation in drug trials more attractive than enrolling in conservative non-pharmacological intervention studies. This preference can hinder the recruitment of participants for future non-pharmacological clinical research,

as this may also make them ineligible. Additionally, RCTs can be cost-prohibitive, and the substantial costs may not align with the priorities of funding bodies, which may prefer to allocate resources to research in more common diseases. While government research councils have offered funding schemes, these opportunities are relatively limited, and industry or charitable organisations often serve as primary research funding sources in this field. Relying on non-governmental sources can complicate building sustainable research infrastructure, requiring innovative funding and collaborative efforts to advance MD research effectively.

A universally agreed core outcome set for evaluating therapy interventions in MD is still lacking. Validated outcome measures specific to MD are often scarce, necessitating the use of measures validated for other conditions. However, differences in disease mechanisms, progression, manifestations and the heterogeneity of MD diseases can compromise the validity of these extrapolated measures. Additionally, outcome measures designed for different clinical populations may lack face validity for some MD subgroups, potentially leading to underestimation of the interventions' significance and inaccurate conclusions regarding effectiveness. The absence of standardised core outcome sets also complicates the intervention effectiveness assessment and hinders meaningful comparisons between studies. Future efforts should focus on developing patient-centred core outcome sets, which should reflect what is important to individuals living with different MD, account for the unique MD progressions, establish clinically meaningful differences and ensure measures are valid and reliable.

Registries and clinical databases serve as valuable tools for gathering data on individuals with NMD.[64] In cases where evidence is scarce, they offer a potentially sustainable approach to determining effectiveness.[65 66] However, their effectiveness depends on the engagement of patient and centres, integration of relevant electronic health records, consideration of measurement burden, appropriate outcome measures inclusion, high data completion rates and regular updates in response to emerging evidence. While existing registries have been used for exploratory research, their utility in informing clinical decision-making has not been fully developed, possibly owing to a failure to address the requirements above.

The scarcity of comprehensive natural history data in MD poses a significant challenge for assessing intervention effectiveness. Without this baseline knowledge, distinguishing intervention effects from natural disease progression is difficult, as exemplified by the challenging interpretation of strength decline following strength training. Additionally, the lack of natural history data affects decisions on intervention timing and duration. Robust natural history studies are necessary to provide insights into disease progression, guide treatment strategies and establish a benchmark for intervention impact evaluation.

Taken together, these actions will enhance research quality, inform guidelines, support healthcare professionals, standardise care across clinical sites and ultimately improve care for individuals with MD.

Strengths

The analysis of the effectiveness of conservative non-pharmacological interventions in MD was comprehensive. This was achieved by search strategies without restrictions on date, language, study designs and outcomes.

Limitations

Most data came from non-RCT studies, which may have limitations such as overestimated treatment effects, uncontrolled designs and small sample sizes. This study focused on the conservative non-pharmacological interventions for the MD physical manifestations, excluding respiratory interventions that however are integral to the non-pharmacological management of these conditions. Included articles predominantly involved adults, and paediatric studies consisted largely of children with DMD, which could limit the applicability of the findings to children with MD forms other than DMD. Limitations also included heterogeneity in the study populations and outcome measures, use of non-validated outcome measures and, in some studies, inclusion of multiple patient populations whose data could not be separated by individual conditions. Future studies should present separate MD group data to identify specific group intervention interactions.

CONCLUSION

This systematic review and meta-analysis indicated that most conservative non-pharmacological interventions produced non-statistically significant treatment effects. Nevertheless, identified interventions did not appear to be harmful. Furthermore, low-quality evidence suggested that supervised strength training, alone or combined with other exercise interventions, may improve perceived exertion, distal arm function, balance, gait and well-being despite no significant structural changes. Therefore, strength training, alone or as part of a multicomponent programme, should be considered as the mainstay in the treatment of MD. Evidence on the effectiveness of assistive technologies, orthotic devices and manual therapy interventions remains limited and inconclusive. Future large-scale, well-designed and well-reported studies are needed to clarify the role of non-pharmacological interventions in MD and to support their clinical use.

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terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

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REFERENCES

1 Theadom A, Rodrigues M, Roxburgh R, *et al*. Prevalence of muscular dystrophies: a systematic literature review. *Neuroepidemiology* 2014;43:259–68.
2 Mercuri E, Bönnemann CG, Muntoni F. Muscular dystrophies. *Lancet* 2019;394:2025–38.
3 Lovering RM, Porter NC, Bloch RJ. The muscular Dystrophies: from genes to therapies. *Phys Ther* 2005;85:1372–88.
4 Mercuri E, Muntoni F. Muscular dystrophies. *Lancet* 2013;381:845–60.
5 Verhaert D, Richards K, Rafael-Fortney JA, *et al*. Cardiac involvement in patients with muscular dystrophies: magnetic resonance imaging phenotype and genotypic considerations. *Circ Cardiovasc Imaging* 2011;4:67–76.
6 Grootenhuis MA, de Boone J, van der Kooi AJ. Living with muscular dystrophy: health related quality of life consequences for children and adults. *Health Qual Life Outcomes* 2007;5:31.
7 Leung DG, Wagner KR. Therapeutic advances in muscular dystrophy. *Ann Neurol* 2013;74:404–11.
8 Cup EH, Pieterse AJ, Ten Broek-Pastoor JM, *et al*. Exercise therapy and other types of physical therapy for patients with neuromuscular diseases: a systematic review. *Arch Phys Med Rehabil* 2007;88:1452–64.
9 Voet NB, van der Kooi EL, van Engelen BG, *et al*. Strength training and aerobic exercise training for muscle disease. *Cochrane Database Syst Rev* 2019;12:CD003907.
10 Pedlow K, McDonough S, Lennon S, *et al*. Assisted standing for duchenne muscular dystrophy. *Cochrane Database Syst Rev* 2019;10:CD011550.
11 Narayanaswami P, Weiss M, Selcen D, *et al*. Evidence-based guideline summary: diagnosis and treatment of limb-girdle and distal dystrophies: report of the guideline development subcommittee of the American academy of neurology and the practice issues review panel of the American association of neuromuscular & electrodiagnostic medicine. *Neurology* 2014;83:1453–63.
12 Moher D, Liberati A, Tetzlaff J, *et al*. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ* 2009;339:b2535.
13 Higgins JPT, Savović J, Page M, *et al*. Assessing risk of bias in a randomized trial. In: Higgins JPT, Thomas J, Chandler J, eds. *Cochrane handbook for systematic reviews of interventions*. 2nd ed. Wiley-Blackwell, 2019: 205–28.
14 Lakens D. Calculating and reporting effect sizes to facilitate cumulative science: a practical primer for t-tests and ANOVAs. *Front Psychol* 2013;4:863.
15 World health organization. *International classification of functioning, disability and health (ICF)*. 2001.
16 Zupan A, Gregorič M, Valenčic V. Long-lasting effects of electrical stimulation upon muscles of patients suffering from progressive muscular dystrophy. *Clin Rehabil* 1995;9:102–9.
17 Hind D, Parkin J, Whitworth V, *et al*. Aquatic therapy for children with duchenne muscular dystrophy: a pilot feasibility randomised controlled trial and mixed-methods process evaluation. *Health Technol Assess* 2017;21:1–120.
18 Carroll K, Yiu EM, Ryan MM, *et al*. The effects of calf massage in boys with duchenne muscular dystrophy: a prospective interventional study. *Disabil Rehabil* 2021;43:3803–9.
19 Colson SS, Benchortane M, Tanant V, *et al*. Neuromuscular electrical stimulation training: a safe and effective treatment for facioscapulohumeral muscular dystrophy patients. *Arch Phys Med Rehabil* 2010;91:697–702.
20 Kierkegaard M, Harms-Ringdahl K, Edström L, *et al*. Feasibility and effects of a physical exercise programme in adults with myotonic dystrophy type 1: a randomized controlled pilot study. *J Rehabil Med* 2011;43:695–702.
21 Missaoui B, Rakotovao E, Bendaya S, *et al*. Posture and gait abilities in patients with myotonic dystrophy (Steinert disease). Evaluation on the short-term of a rehabilitation program. *Ann Phys Rehabil Med* 2010;53:387–98.
22 Kilinç M, Yildirim SA, Tan E. The effects of electrical stimulation and exercise therapy in patients with limb girdle muscular dystrophy: a controlled clinical trial. *Neurosciences (Riyadh)* 2015;20:259–66.
23 Okkersen K, Jimenez-Moreno C, Wenninger S, *et al*. Cognitive behavioural therapy with optional graded exercise therapy in patients with severe fatigue with myotonic dystrophy type 1: a multicentre, single-blind, randomised trial. *Lancet Neurol* 2018;17:671–80.
24 Voet N, Bleijenberg G, Hendriks J, *et al*. Both aerobic exercise and cognitive-behavioral therapy reduce chronic fatigue in FSHD. *Neurology* 2014;83:1914–22.
25 Bostock EL, O'Dowd DN, Payton CJ, *et al*. The effects of resistance exercise training on strength and functional tasks in adults with limb-girdle, becker, and facioscapulohumeral dystrophies. *Front Neurol* 2019;10:1216.
26 Roussel M-P, Hébert LJ, Duchesne E. Strength-training effectively alleviates skeletal muscle impairments in myotonic dystrophy type 1. *Neuromuscul Disord* 2020;30:283–93.
27 Lessard I, Gaboury S, Gagnon C, *et al*. Effects and acceptability of an individualized home-based 10-week training program in adults with myotonic dystrophy type 1. *J Neuromuscul Dis* 2021;8:137–49.
28 Maghbouli N, Shirzad N, Fateh HR, *et al*. Efficacy of a 6-week supervised strengthening exercise program with emg-biofeedback in patients with muscular dystrophy: a randomized controlled trial. *Muscle Ligaments Tendons J* 2021;11:728.
29 Jansen M, van Alfen N, Geurts ACH, *et al*. Assisted bicycle training delays functional deterioration in boys with duchenne muscular dystrophy: the randomized controlled trial "no use Is disuse" *Neurorehabil Neural Repair* 2013;27:816–27.
30 Heutinck L, Jansen M, van den Elzen Y, *et al*. Virtual reality computer gaming with dynamic arm support in boys with duchenne muscular dystrophy. *J Neuromuscul Dis* 2018;5:359–72.
31 Brooke MH, Griggs RC, Mendell JR, *et al*. Clinical trial in duchenne dystrophy. I. The design of the protocol. *Muscle Nerve* 1981;4:186–97.
32 Sherief A, Abd ElAziz HG, Ali MS. Efficacy of two intervention approaches on functional walking capacity and balance in children with duchene muscular dystrophy. *J Musculoskelet Neuronal Interact* 2021;21:343–50.
33 Bankolé L-C, Millet GY, Temesi J, *et al*. Safety and efficacy of a 6-month home-based exercise program in patients with facioscapulohumeral muscular dystrophy: a randomized controlled trial. *Medicine (Baltimore)* 2016;95:e4497.
34 Güneş Gencer GY, Yilmaz Ö. The effect of trunk training on trunk control, upper extremity, and pulmonary function in children with duchenne muscular dystrophy: a randomized clinical trial. *Clin Rehabil* 2022;36:369–78.
35 Kenis-Coskun O, Imamoglu S, Karamancioglu B, *et al*. Comparison of telerehabilitation versus home-based video exercise in patients with duchenne muscular dystrophy: a single-blind randomized study. *Acta Neurol Belg* 2022;122:1269–80.
36 Alemdaroğlu I, Karaduman A, Yilmaz ÖT, *et al*. Different types of upper extremity exercise training in duchenne muscular dystrophy: effects on functional performance, strength, endurance, and ambulation. *Muscle Nerve* 2015;51:697–705.
37 Lindeman E, Leffers P, Spaans F, *et al*. Strength training in patients with myotonic dystrophy and hereditary motor and sensory neuropathy: a randomized clinical trial. *Arch Phys Med Rehabil* 1995;76:612–20.
38 Bulut N, Karaduman A, Alemdaroğlu-Gürbüz İ, *et al*. The effect of aerobic training on motor function and muscle architecture in children with duchenne muscular dystrophy: a randomized controlled study *Clin Rehabil* 2022;36:1062–71.
39 Aldehag A, Jonsson H, Lindblad J, *et al*. Effects of hand-training in persons with myotonic dystrophy type 1-a randomised controlled cross-over pilot study. *Disabil Rehabil* 2013;35:1798–807.
40 O'Dowd DN, Bostock EL, Smith D, *et al*. The effects of 12 weeks' resistance training on psychological parameters and quality of life in adults with facioscapulohumeral, becker, and limb–girdle dystrophies. *Disabil Rehabil* 2022;44:5950–6.
41 Ribot-Ciscar E, Milhe-De Bovis V, Aimonetti J-M, *et al*. Functional impact of vibratory proprioceptive assistance in patients with facioscapulohumeral muscular dystrophy. *Muscle Nerve* 2015;52:780–7.
42 Glanzman AM, Flickinger JM, Dholakia KH, *et al*. Serial casting for the management of ankle contracture in duchenne muscular dystrophy. *Pediatr Phys Ther* 2011;23:275–9.
43 Aprile I, Bordieri C, Gilardi A, *et al*. Balance and walking involvement in facioscapulohumeral dystrophy: a pilot study on the effects of custom lower limb orthoses. *Eur J Phys Rehabil Med* 2013;49:169–78.
44 Taktak DM, Bowker P. Lightweight, modular knee-ankle-foot orthosis for duchenne muscular dystrophy: design, development, and evaluation. *Arch Phys Med Rehabil* 1995;76:1156–62.
45 Vry J, Schubert IJ, Semler O, *et al*. Whole-body vibration training in children with duchenne muscular dystrophy and spinal muscular atrophy. *Eur J Paediatr Neurol* 2014;18:140–9.
46 Chisari C, Bertolucci F, Dalise S, *et al*. Chronic muscle stimulation improves muscle function and reverts the abnormal surface EMG pattern in myotonic dystrophy: a pilot study. *J Neuroeng Rehabil* 2013;10:94.
47 Pegoraro V, Cudia P, Baba A, *et al*. Myomirnas and myostatin as physical rehabilitation biomarkers for myotonic dystrophy. *Neurol Sci* 2020;41:2953–60.
48 Hammarén E, Lindberg C, Kjellby-Wendt G. Effects of a balance exercise programme in myotonic dystrophy type 1: a pilot study. *Eur J Physiother* 2015;17:123–31.
49 Tollbäck A, Eriksson S, Wredenberg A, *et al*. Effects of high resistance training in patients with myotonic dystrophy. *Scand J Rehabil Med* 1999;31:9–16.
50 Berthelsen MP, Husu E, Christensen SB, *et al*. Anti-gravity training improves walking capacity and postural balance in patients with muscular dystrophy. *Neuromuscul Disord* 2014;24:492–8.
51 Jensen BR, Berthelsen MP, Husu E, *et al*. Body weight-supported training in becker and limb girdle 2I muscular dystrophy. *Muscle Nerve* 2016;54:239–43.
52 Kontou E, Papadopoulos C, Papadimas G, *et al*. Effect of exercise training on functional capacity and body composition in myotonic dystrophy type 2 patients. *Muscle Nerve* 2021;63:477–83.

53 Orngreen MC, Olsen DB, Vissing J. Aerobic training in patients with myotonic dystrophy type 1. *Ann Neurol* 2005;57:754–7.
54 Sveen ML, Jeppesen TD, Hauerslev S, *et al*. Endurance training improves fitness and strength in patients with becker muscular dystrophy. *Brain* 2008;131(Pt 11):2824–31.
55 Mikhail AI, Nagy PL, Manta K, *et al*. Aerobic exercise elicits clinical adaptations in myotonic dystrophy type 1 patients independently of pathophysiological changes. *J Clin Invest* 2022;132:e156125.
56 Voet NBM. Exercise in neuromuscular disorders: a promising intervention. *Acta Myol* 2019;38:207–14.
57 Michie S, van Stralen MM, West R. The behaviour change wheel: a new method for characterising and designing behaviour change interventions. *Implement Sci* 2011;6:42.
58 Van den Bergh PYK, van Doorn PA, Hadden RDM, *et al*. European academy of neurology/peripheral nerve society guideline on diagnosis and treatment of chronic inflammatory demyelinating polyradiculoneuropathy: report of a joint task force-second revision. *J Peripher Nerv Syst* 2021;26:242–68.
59 Nierse CJ, Abma TA, Horemans AMC, *et al*. Research priorities of patients with neuromuscular disease. *Disabil Rehabil* 2013;35:405–12.
60 Connor SG, Fairchild TJ, Learmonth YC, *et al*. Testosterone treatment combined with exercise to improve muscle strength, physical function and quality of life in men affected by inclusion body myositis: a randomised, double-blind, placebo-controlled, crossover trial. *PLoS One* 2023;18:e0283394.
61 van der Kooi EL, Vogels OJM, van Asseldonk R, *et al*. Strength training and albuterol in facioscapulohumeral muscular dystrophy. *Neurology* 2004;63:702–8.
62 Jacques MF, Stockley RC, Bostock EI, *et al*. Frequency of reported pain in adult males with muscular dystrophy. *PLoS One* 2019;14:e0212437.
63 Jensen MP, Hoffman AJ, Stoelb BL, *et al*. Chronic pain in persons with myotonic dystrophy and facioscapulohumeral dystrophy. *Arch Phys Med Rehabil* 2008;89:320–8.
64 Lofra RM, Walker H, Turner C, *et al*. P200 The UK myotonic dystrophy patient registry - empowering clinical research and patient voice with an effective translational research tool. *Neuromuscul Disord* 2023;33:S144.
65 Harvey S, Rowan K, Harrison D, *et al*. Using clinical databases to evaluate healthcare interventions. *Int J Technol Assess Health Care* 2010;26:86–94.
66 Schwartz MH, Ries AJ. Rectus femoris transfer in children with cerebral palsy: comparing a propensity score-matched observational study to a randomized controlled trial. *Dev Med Child Neurol* 2021;63:196–203.

Supplementary file 1. Search strategies

The PICO (Population, Intervention, Comparison and Outcome) model was used to develop the different search strategies. A series of free-text and MeSH terms, which were combined using Boolean operators, were used for the following keywords: “Muscular dystrophies” AND “Physical management”. The set of free-text terms for “physical management” included terms referring to conservative non-pharmacological treatments used to treat the physical manifestations associated with MD, such as physical as well as occupational therapy modalities and orthotic devices. No language limits were applied.

MEDLINE search strategy			
PICO	**Search terms**	**Mesh headings**	**Free text**
Population	Muscular dystrophies	“Muscular dystrophies”	“Muscular dystrophy” OR “muscular dystrophies” OR “MD” OR “myotonic dystrophy” OR “myotonic dystrophies” OR “facioscapulohumeral muscular dystrophy” OR “FSHD” OR “Duchenne muscular dystrophy” OR “DMD” OR “Becker muscular dystrophy” OR “Becker MD” OR “BMD” OR “Limb-girdle muscular dystrophy” OR “LGMD” OR “congenital muscular dystrophy” OR “CMD” OR “Emery-Dreifuss muscular dystrophy” OR “EDMD”
Intervention	Physical management	“Conservative treatment”, “Physical therapy modalities”, “Occupational therapy”, “Orthotic devices”	(Physical OR conservative OR nonsurgical OR non-surgical OR nonoperative OR non-operative OR nonpharmacological OR non-pharmacological) AND (management OR therapy OR treatment OR approach* OR intervention) Rehabilitation OR “rehabilitation modalit*” OR “rehabilitation technique*” OR “physical therapy modalit*” OR “physical therapy technique*” OR “physical therapy management” OR “physical rehabilitation” OR “physical rehabilitation approach*” OR physiotherapy OR kinesiotherapy OR “occupational therapy modalit*” OR “occupational therapy technique*” OR “occupational therapy” OR “occupational therapy approach*” Exercise* OR “exercise program*” OR “exercise training” OR “exercise therapy” OR “physical exercise*” OR “therapeutic exercise*” OR “physical activity” OR “physical training” OR “training program*” OR “muscle training” OR “muscle exercise*” OR “resistance training” OR “strength training” OR “muscle strengthening exercise*” OR “resistive exercise*” OR “resistive training” OR “manual therapy” OR “manual therapy technique*” OR “manipulative therap*” OR “aerobic training” OR “aerobic exercise*” OR “endurance exercise*” OR “endurance training” OR hydrotherapy OR “acquatic therapy” OR “acquatic physical therapy” OR stretch* OR “stretching exercise*” brace* OR bracing OR “serial casting” OR orthotic* OR orthosis OR orthoses OR “orthopedic equipment” OR “adaptive equipment” OR “assistive equipment” OR “adaptive device*” OR “assistive device*” OR “orthopedic device*” OR “orthotic device*” OR “orthotic intervention*” OR splint* OR “standing device*” OR “assistive technology”
Comparison	N/A		
Outcome	All outcomes		
Study design	All study designs		

CINHAL search strategy			
PICO	**Search terms**	**Mesh headings**	**Free text**
Population	Muscular dystrophies	"Muscular dystrophy"	"Muscular dystrophy" OR "muscular dystrophies" OR "MD" OR "myotonic dystrophy" OR "myotonic dystrophies" OR "facioscapulohumeral muscular dystrophy" OR "FSHD" OR "Duchenne muscular dystrophy" OR "DMD" OR "Becker muscular dystrophy" OR "Becker MD" OR "BMD" OR "Limb-girdle muscular dystrophy" OR "LGMD" OR "congenital muscular dystrophy" OR "CMD" OR "Emery-Dreifuss muscular dystrophy" OR "EDMD"
Intervention	Physical management	"Physical therapy" "Occupational therapy" "Orthopedic equipment and supplies"	(Physical OR conservative OR nonsurgical OR non-surgical OR nonoperative OR non-operative OR nonpharmacological OR non-pharmacological) AND (management OR therapy OR treatment OR approach* OR intervention) Rehabilitation OR "rehabilitation modalit*" OR "rehabilitation technique*" OR "physical therapy modalit*" OR "physical therapy technique*" OR "physical therapy management" OR "physical rehabilitation" OR "physical rehabilitation approach*" OR physiotherapy OR kinesiotherapy OR "occupational therapy modalit*" OR "occupational therapy technique*" OR "occupational therapy" OR "occupational therapy approach*" Exercise* OR "exercise program*" OR "exercise training" OR "exercise therapy" OR "physical exercise*" OR "therapeutic exercise*" OR "physical activity" OR "physical training" OR "training program*" OR "muscle training" OR "muscle exercise*" OR "resistance training" OR "strength training" OR "muscle strengthening exercise*" OR "resistive exercise*" OR "resistive training" OR "manual therapy" OR "manual therapy technique*" OR "manipulative therap*" OR "aerobic training" OR "aerobic exercise*" OR "endurance exercise*" OR "endurance training" OR hydrotherapy OR "acquatic therapy" OR "acquatic physical therapy" OR stretch* OR "stretching exercise*" Brace* OR bracing OR "serial casting" OR orthotic* OR orthosis OR orthoses OR "orthopedic equipment" OR "adaptive equipment" OR "assistive equipment" OR "adaptive device*" OR "assistive device*" OR "orthopedic device*" OR "orthotic device*" OR "orthotic intervention*" OR splint* OR "standing device*" OR "assistive technology"
Comparison	N/A		
Outcome	All outcomes		
Study design	All study designs		

EMBASE search strategy		
PICO	**Search terms**	**Free text**
Population	Muscular dystrophies	"Muscular dystrophy" OR "muscular dystrophies" OR "MD" OR "myotonic dystrophy" OR "myotonic dystrophies" OR "facioscapulohumeral muscular dystrophy" OR "FSHD" OR "Duchenne muscular dystrophy" OR "DMD" OR "Becker muscular dystrophy" OR "Becker MD" OR "BMD" OR "Limb-girdle muscular dystrophy" OR "LGMD" OR "congenital muscular dystrophy" OR "CMD" OR "Emery-Dreifuss muscular dystrophy" OR "EDMD"
Intervention	Physical management	(Physical OR conservative OR nonsurgical OR non-surgical OR nonoperative OR non-operative OR nonpharmacological OR non-pharmacological) AND (management OR therapy OR treatment OR approach* OR intervention) Rehabilitation OR "rehabilitation modalit*" OR "rehabilitation technique*" OR "physical therapy modalit*" OR "physical therapy technique*" OR "physical therapy management" OR "physical rehabilitation" OR "physical rehabilitation approach*" OR physiotherapy OR kinesiotherapy OR "occupational therapy modalit*" OR "occupational therapy technique*" OR "occupational therapy" OR "occupational therapy approach*" Exercise* OR "exercise program*" OR "exercise training" OR "exercise therapy" OR "physical exercise*" OR "therapeutic exercise*" OR "physical activity" OR "physical training" OR "training program*" OR "muscle training" OR "muscle exercise*" OR "resistance training" OR "strength training" OR "muscle strengthening exercise*" OR "resistive exercise*" OR "resistive training" OR "manual therapy" OR "manual therapy technique*" OR "manipulative therap*" OR "aerobic training" OR "aerobic exercise*" OR "endurance exercise*" OR "endurance training" OR hydrotherapy OR "acquatic therapy" OR "acquatic physical therapy" OR stretch* OR "stretching exercise*" Brace* OR bracing OR "serial casting" OR orthotic* OR orthosis OR orthoses OR "orthopedic equipment" OR "adaptive equipment" OR "assistive equipment" OR "adaptive device*" OR "assistive device*" OR "orthopedic device*" OR "orthotic device*" OR "orthotic intervention*" OR splint* OR "standing device*" OR "assistive technology"
Comparison	N/A	
Outcome	All outcomes	
Study design	All study designs	

AMED search strategy	
PICO	**Free text**
Population	"Muscular dystrophy" OR "muscular dystrophies" OR "MD" OR "myotonic dystrophy" OR "myotonic dystrophies" OR "facioscapulohumeral muscular dystrophy" OR "FSHD" OR "Duchenne muscular dystrophy" OR "DMD" OR "Becker muscular dystrophy" OR "Becker MD" OR "BMD" OR "Limb-girdle muscular dystrophy" OR "LGMD" OR "congenital muscular dystrophy" OR "CMD" OR "Emery-Dreifuss muscular dystrophy" OR "EDMD"
Intervention	(Physical OR conservative OR nonsurgical OR non-surgical OR nonoperative OR non-operative OR nonpharmacological OR non-pharmacological) AND (management OR therapy OR treatment OR approach* OR intervention) Rehabilitation OR "rehabilitation modalit*" OR "rehabilitation technique*" OR "physical therapy modalit*" OR "physical therapy technique*" OR "physical therapy management" OR "physical rehabilitation" OR "physical rehabilitation approach*" OR physiotherapy OR kinesiotherapy OR "occupational therapy modalit*" OR "occupational therapy technique*" OR "occupational therapy" OR "occupational therapy approach*" Exercise* OR "exercise program*" OR "exercise training" OR "exercise therapy" OR "physical exercise*" OR "therapeutic exercise*" OR "physical activity" OR "physical training" OR "training program*" OR "muscle training" OR "muscle exercise*" OR "resistance training" OR "strength training" OR "muscle strengthening exercise*" OR "resistive exercise*" OR "resistive training" OR "manual therapy" OR "manual therapy technique*" OR "manipulative therap*" OR "aerobic training" OR "aerobic exercise*" OR "endurance exercise*" OR "endurance training" OR hydrotherapy OR "acquatic therapy" OR "acquatic physical therapy" OR stretch* OR "stretching exercise*" Brace* OR bracing OR "serial casting" OR orthotic* OR orthosis OR orthoses OR "orthopedic equipment" OR "adaptive equipment" OR "assistive equipment" OR "adaptive device*" OR "assistive device*" OR "orthopedic device*" OR "orthotic device*" OR "orthotic intervention*" OR splint* OR "standing device*" OR "assistive technology"
Comparison	N/A
Outcome	All outcomes
Study design	All study designs

The Cochrane Central Register of Controlled Trials (CENTRAL)			
PICO	**Search terms**	**Mesh headings**	**Free text**
Population	Muscular dystrophies	"Muscular dystrophies" (explode all trees)	"Muscular dystrophy" OR "muscular dystrophies" OR "MD" OR "myotonic dystrophy" OR "myotonic dystrophies" OR "facioscapulohumeral muscular dystrophy" OR "FSHD" OR "Duchenne muscular dystrophy" OR "DMD" OR "Becker muscular dystrophy" OR "Becker MD" OR "BMD" OR "Limb-girdle muscular dystrophy" OR "LGMD" OR "congenital muscular dystrophy" OR "CMD" OR "Emery-Dreifuss muscular dystrophy" OR "EDMD"
Intervention	Physical management	"Conservative treatment" (single mesh term unexploded), Rehabilitation (explode all trees), Orthoses (explode all trees)	(Physical OR conservative OR nonsurgical OR non-surgical OR nonoperative OR non-operative OR nonpharmacological OR non-pharmacological) AND (management OR therapy OR treatment OR approach* OR intervention) Rehabilitation OR "rehabilitation modalit*" OR "rehabilitation technique*" OR "physical therapy modalit*" OR "physical therapy technique*" OR "physical therapy management" OR "physical rehabilitation" OR "physical rehabilitation approach*" OR physiotherapy OR kinesiotherapy OR "occupational therapy modalit*" OR "occupational therapy technique*" OR "occupational therapy" OR "occupational therapy approach*" Exercise* OR "exercise program*" OR "exercise training" OR "exercise therapy" OR "physical exercise*" OR "therapeutic exercise*" OR "physical activity" OR "physical training" OR "training program*" OR "muscle training" OR "muscle exercise*" OR "resistance training" OR "strength training" OR "muscle strengthening exercise*" OR "resistive exercise*" OR "resistive training" OR "manual therapy" OR "manual therapy technique*" OR "manipulative therap*" OR "aerobic training" OR "aerobic exercise*" OR "endurance exercise*" OR "endurance training" OR hydrotherapy OR "acquatic therapy" OR "acquatic physical therapy" OR stretch* OR "stretching exercise*" Brace* OR bracing OR "serial casting" OR orthotic* OR orthosis OR orthoses OR "orthopedic equipment" OR "adaptive equipment" OR "assistive equipment" OR "adaptive device*" OR "assistive device*" OR "orthopedic device*" OR "orthotic device*" OR "orthotic intervention*" OR splint* OR "standing device*" OR "assistive technology"
Comparison	N/A		
Outcome	All outcomes		
Study design	All study designs		

Supplementary file 2. Framework for data extraction process

Data extraction framework
Authors
Year of publication
Country of publication
Study design
Sample size
Participant demographics
Study setting
Conservative non-pharmacological Intervention characteristics (FITT principles) • Intervention frequency • Target intensity • Intervention duration • Type of intervention
Outcome measures pertaining the following domains (based on the ICF framework) • Body function* • Body structure** • Activities and participation*** • Pain
Presence of supervision
Adherence
Attrition rate
Adverse events

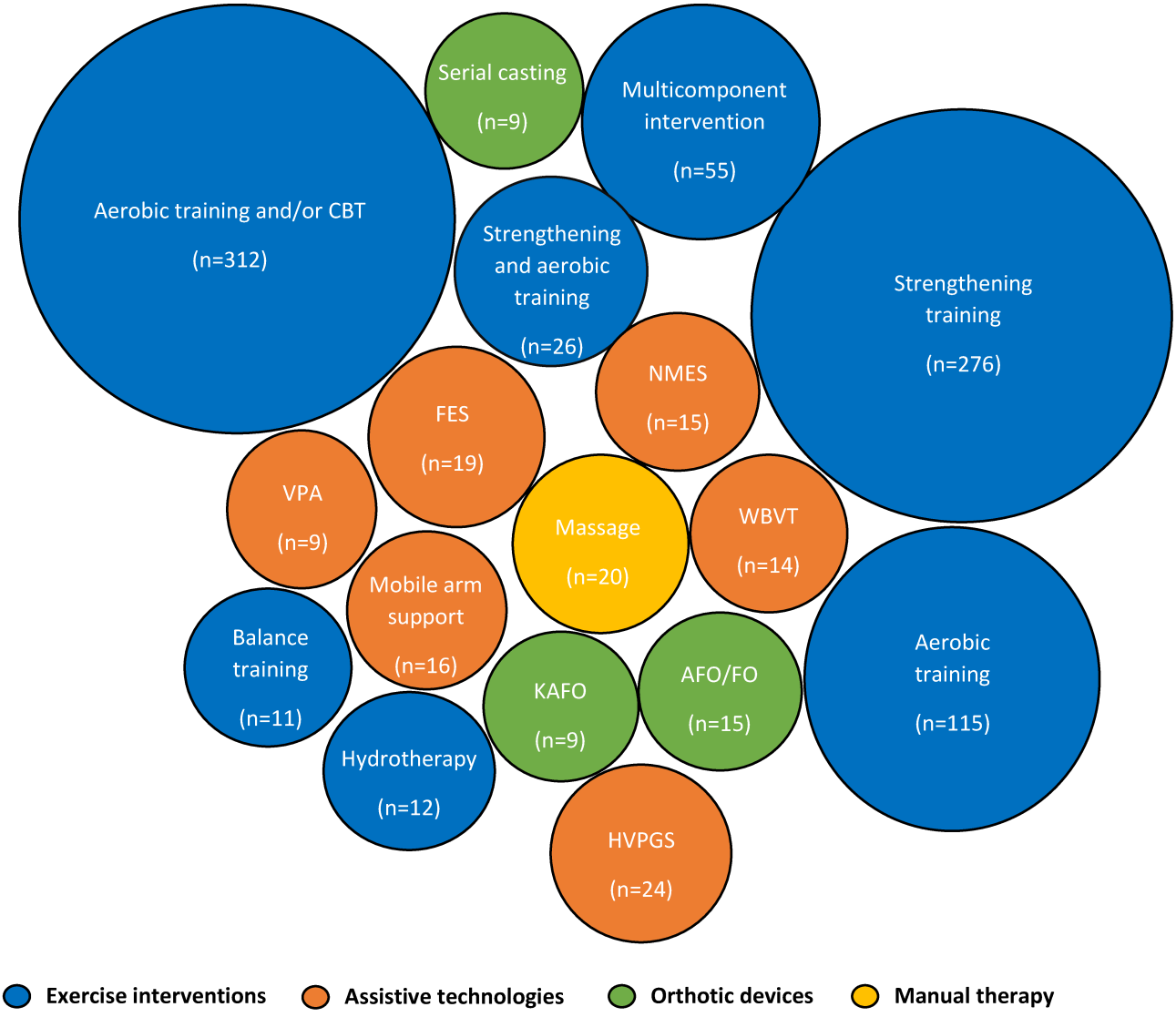
Abbreviations: FITT, Frequency, Intensity, Time, and Type; ICF, International Classification of Functioning, Disability and Health

Notes:
*Comprised objective outcome measures assessing the body physiological functions. Outcome measures pertaining molecular biomarkers and histological as well as muscle biopsy parameters were not extracted for the purpose of this study
**Comprised objective outcome measures assessing the anatomical parts of the body
***Comprised objective and patient-reported outcomes measuring patients' difficulties in executing tasks and activities

Supplementary file 3. Effect size calculation

Mean difference and pooled Standard Deviation (SD) were calculated using the mean values and SDs provided in each of the studies. When mean values and SDs were missing and could not be obtained from the authors, they were calculated, where possible, from reported standard errors and participant data. In cross-over studies, we extracted data from the time period prior to the introduction of the cross-over design. In before-after studies with control group, if data from either study group were not in the correct format for analysis, were not reported in the publication or had not been collected as part of the study protocol, data extraction was only performed for the study group for which usable data were available. Follow-up data was not extracted if treatment was discontinued. If studies included derived outcomes that were correlated with other outcomes, we reported the most direct outcome measures. Outcome measures were omitted if their psychometric properties were not satisfactory.

Supplementary file 4. Number of participants in each intervention type



Abbreviations: CBT, Cognitive Behavioural Therapy; VPA, Vibratory Proprioceptive Assistance; FES, Functional Electrical Stimulation; NMES, Neuromuscular Electrical Stimulation; WBVT, Whole-Body Vibration Training; HVPGS, High Voltage Pulsed Galvanic Stimulation; KAFO, Knee-Ankle-Foot Orthosis; AFO, Ankle Foot Orthosis; FO; Foot orthosis.

Supplementary file 5. Characteristics of the included studies

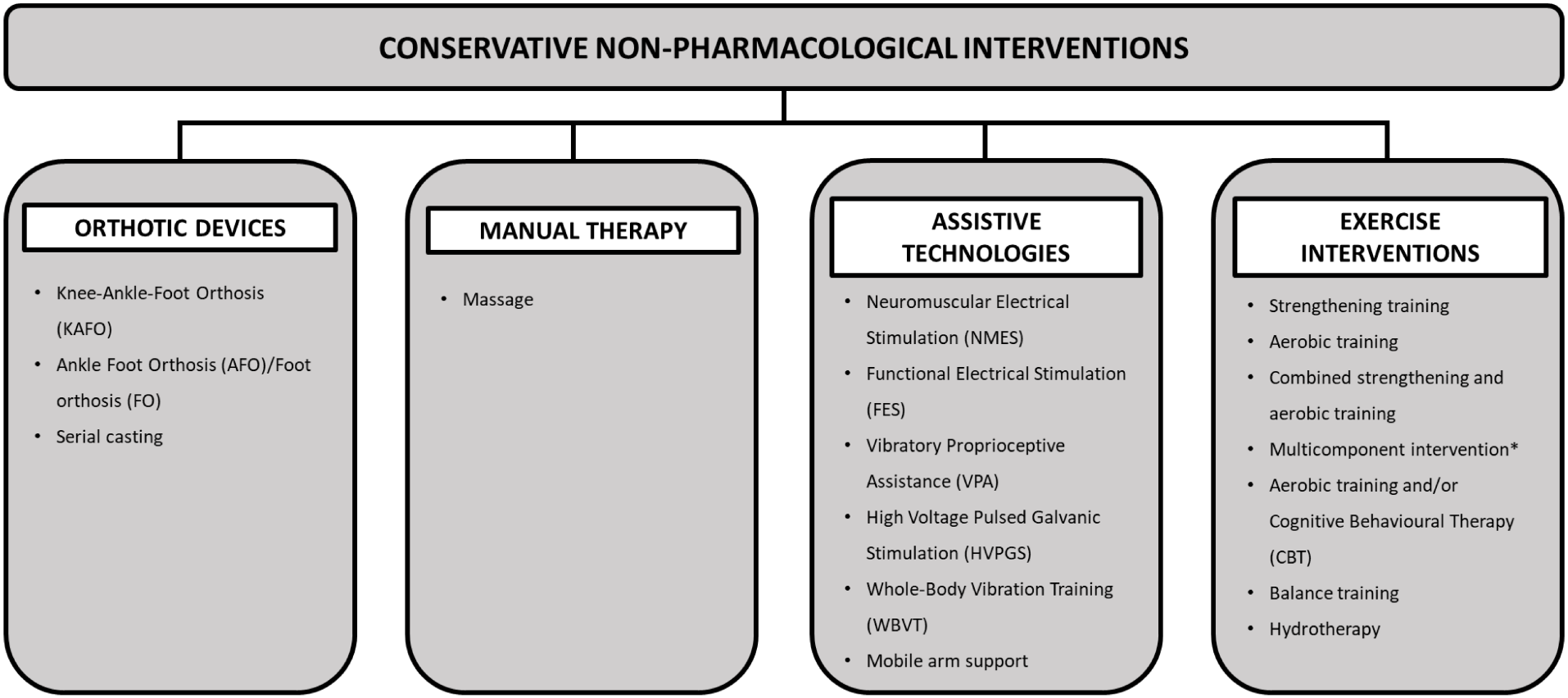
Authors	Year	Country	Study design	MD type(s)	Participant characteristics
Orthotic devices					
Glanzman et al. [42]	2011	USA	Case series	DMD	n=9 (M), mean age: 8.9 ±2.1 years; IC: ability to rise from the floor independently, lacking ROM to neutral dorsiflexion and/or habitual toe walkers
Aprile et al. [43]	2013	Italy	Before-after study (no CG)	FSHD	n=15 (F: n=11; M, n=4), mean age 47.3±16.7 years; IC: CSS grade 2.5-4 grade
Taktak et al. [44]	1995	UK	Before-after study (no CG)	DMD	n=9 (M), age range: 5-13 years
Manual therapy					
Carroll et al. [18]	2020	Australia	Crossover study	DMD	n=20 (M), mean age: 9.3 years (range: 8.0–10.5 years); IC: ability to walk independently (> 10 m) and to lay prone (> 10 min)
Assistive technologies					
Heutinck et al. [30]	2018	Netherlands	RCT	DMD	n=16 (M); SG, n=7, mean age: 12.9±2.8 years; CG, n=9, mean age: 12.6±3.4 years; IC: inability to walk and impaired arm function (grade 2-4 Brooke Upper Extremity Scale)
Vry et al. [45]	2014	Germany	Before-after study (no CG)	DMD	n=14 (M), mean age: 8.8 years; IC: ability to walk unaided (≥ 10 m)
Pegoraro et al. [47]	2020	Italy	Before-after study (no CG)	DM1	n=9 (F: n=1; M, n=8), mean age: 47 years (range: 38-67 years); IC: MIRS grade 2+ and tibialis anterior muscle strength <4 MRC scale
Zupan et al. [16]	1995	Slovenia	Before-after trial (with CG)	DMD, BMD, LGMD, FSHD	n=10 (DMD, n=2; BMD, n=3; LGBMD, n=3; FSHD, n=1), mean age: 14.3±4.3 years
Chisari et al. [46]	2013	Italy	Before-after study (no CG)	DM1, CMD	n=6; DM1: n=5 (F: n=2; M: n=3), age range: 28-65 years; CMD: n=1, gender not specified, age: 39
Colson et al. [44]	2010	France	Before-after study (no CG)	FSHD	n=9 (F: n=3; M, n=6), mean age: 55.21 years; IC: quadriceps femoris muscle weakness and ability to walk unaided (Vignos scale ≤5)
Kilinç et al. [22]	2015	Turkey	Before-after trial (with CG)	LGMD	n=24 (F, n=5; M, n=19); Electrical stimulation group, n=11; mean age: 31.62±16.92 years; Exercise group, n=13; mean age: 30.14±11.04 years; IC: ability to walk without assistive devices and muscle strength grade 3+ (MRC scale)
Ribot-Ciscar et al. [41]	2015	France	Before-after study (no CG)	FSHD	n=9 (F, n=6; M, n=3), mean age: 58±11 years; IC: preserved shoulder abduction and Brooke Upper Extremity Scale grade 2-4

Exercise interventions					
Authors	**Year**	**Country**	**Study design**	**MD type(s)**	**Participant characteristics**
				Aerobic training	
Bulut et al. [38]	2022	Turkey	RCT	DMD	n=21; SG: n=10, median age: 7.9 years (7.2, 8.7), CG: n=11, median age: 8.6 years (7.9, 10.1); IC: grade 1-2 Vignos Scale
Sherief et al. [32]	2021	Egypt	RCT	DMD	n=30 (M); Group A, n=15; mean age: 8.34 ± 0.88 years; Group B, n=15; mean age: 8.49 ± 0.83 years; IC: grade 3+ MRC scale (lower limbs and trunk); sufficient functional upper and lower limb ROMs; and level I and II AFCSD
Bankolé et al. [33]	2016	France	RCT	FSHD	n=19; SG: n=10 (F, n=4; M, n=6); CG: n=9 (F, n=1; M, n=8). 16 participants completed the study. 8 in CG (F, n=1; M, n=7, mean age: 41±9 yeas), 8 in SG (F, n=3; M, n=5, mean age: 40±13 years)
Mikhall et al. [55]	2022	Canada	Before-after study (no CG)	DM1	n=22; SG, n=11 (F, n=6; M, n=5), mean age: 42.6±3 years; CG, n=11 (F, n=6; M, n=5), mean age: 42.5±2 years
Sveen et al. [54]	2008	Denmark	Before-after study (no CG)	BMD	n=11 (M), mean age: 32 ± 4 years
Orngreen et al. [53]	2005	Denmark	Before-after study (no CG)	DM1	n=12 (F, n=3; M, n=9); age range: 21-58 years
				Aerobic training and/or cognitive behavioural therapy	
Okkersen et al. [23]	2018	France, Germany, UK and Netherlands	RCT	DM1	n=255; SG: n=128 (F, n=58; M, n=70, mean age: 44.8±11.7 years; CG, n=127 (F, n=60; M, n=67), mean age: 46.4±11.3 years. IC: ability to walk independently (walking aids permitted)
Voet et al. [24]	2014	Netherlands	RCT	FSHD	n=57; CBT: n=13 (F, n=5; M, n=8) median age: 49 years (range: 24-69 years); ATG: n=20 (F, n=8; M, n=12) median age: 59 years (range: 21-68 years); CG, n=24 (F, n=17; M, n=17), median age: 52 years (range: 20-79 years). IC: ability to walk independently (orthoses and walking aids permitted)
				Strength and aerobic training	
Kontou et al. [52]	2020	Greece	Before-after study (no CG)	DM2	n=10 (F, n=3; M, n=7), mean age: 63.0 ± 8.3 years; IC: ability to walk
Jensen et al. [51]	2016	Denmark	Before-after study (no CG)	BMD, LGMD type 2I	n=8; BMD: n=5 (M); LGMD2I: n=3 (F, n=2; M, n=1); mean age: 36 ± 4 years; IC: ability to stand/walk, but inability to exercise unsupervised (e.g., running, cycling)
Berthelsen et al. [50]	2014	Denmark	Before-after study (no CG)	BMD, LGMD type 2I	n=8; BMD: n=5 (M); LGMD2I: n=3 (F, n=2; M, n=1); mean age: 36 ± 4 years; IC: ability to stand/walk, but inability to exercise unsupervised (e.g., running, cycling)
				Strength training	
Güneş Gencer et al. [34]	2022	Turkey	RCT	DMD	n=26 (M); SG: n=13, mean age: 11.6 ± 2.6 years; CG: n=13, mean age: 10.6±3.4 years
Kenis-Coskun et al. [35]	2022	Turkey	RCT	DMD	n=22 (M); SG: n=10, mean age: 8.80 ± 2.93 years; CG: n=12, mean age: 7.00±2.00 years; IC: ability to walk
Maghbouli et al. [28]	2021	Iran	RCT	MD (subtype not specified)	n=40; SG, n=20 (F, n=6; M, n=14), mean age: 37.3±1.8 years; CG, n=20 (F, n=5; M, n=15), mean age: 31.2±5.5 years. IC: ability to walk (≥ 10 m) (walking aids permitted)
Alemdaroglu et al. [36]	2015	Turkey	RCT	DMD	n=24 (M), age range: 8–12 years; SG; n=12, mean age: 9.50±1.38 years; CG: n=12, mean age: 9.33±1.37 years. IC: grade 1-3 Brooke Upper Extremity scale
Aldehag et al. [39]	2013	Sweden	RCT (with cross-over design)	DM1	n=35 (F, n=21; M, n=14); mean age: 46 years, range: 26-69 years; Group A: n=18 (F: n=5; M, n=13); Group B: n=17 (F, n=8; M, n=9). IC: MRC scale grade 3+ (wrist and hand muscles)
Jansen et al. [29]	2013	Netherlands	RCT	DMD	n=30 (M), mean age: 10.5±2.6 years; SG: n=17, mean age: 10.8±2.4 years; CG: n=13, mean age: 10.5±2.8 years. IC: ambulant individuals with impaired gait and/or difficulties with rising from the floor; wheelchair-dependent individuals able to touch the top of their head with both hands, or able to use a hand-operated wheelchair
Lindeman et al. [37]	1995	Netherlands	RCT	MD (subtype not specified)	n=30; SG: n=15 (F, n=6; M, n=9), mean age: 40±11years (range:18-57 years); CG: n=15 (F, n=3; M, n=12), mean age: 37±10 years (range: 20-55 years)
O'Dowd et al. [40]	2022	UK	Before-after study (no CG)	FSHD, LGMD, BMD	n=17 (F, n=13; M, n=7), mean age: 44±11 years; FSHD: n=6 (F, n=2; M, n=4), mean age: 43±12 years; LGMD: n=6 (F: n=2; M: n=4), mean age: 47±11; BMD: n=5, mean age: 40±8 years; IC: ability to walk (≥ 7 m) (walking aids permitted)
Lessard et al. [27]	2021	Canada	Before-after study (no CG)	DM1	n=15 (M), mean age: 47.7±10.9 years (range: 28-62 years)
Roussel et al. [26]	2020	Canada	Before-after study (no CG)	DM1	n=11 (M), age range: 30-65 years. IC: ability to walk without assistance

Bostock et al. [25]	2019	UK	Before-after study (no CG)	LGMD, BMD, FSHD	n=17 (F, n=4; M, n=13), mean age: 44±11 years; LGMD, n=6; BMD, n=5; FSHD, n=6. IC: ability to walk (≥ 7 m) (walking aids permitted)
Tollbäck et al. [49]	1999	Sweden	Before-after trial (with CG)	MD (subtype not specified)	n=9 (F, n=7; M, n=2), mean age: 37±8.6 years; IC: ability to walk and to fully extend the knee against a 3 kg load
Hydrotherapy					
Hind et al. [17]	2017	UK	RCT	DMD	n=12; median age: 8.0 years (7.5, 9.5); SG: n=8, mean age: 8.0±0.9 years; CG: n=4; mean age: 9.8±2.5 years. IC: ability to walk (≥ 10 m) without aids/assistance and NSAA score of 8–34
Balance training					
Hammarén et al. [48]	2015	Sweden	Before-after study (no CG)	DM1	n=11 (F, n=3; M, n=8), mean age: 49 (range: 36-60 years)
Multicomponent intervention					
Kierkegaard et al. [20]	2011	Sweden	RCT	DM1	n=35; SG: n=18 (F, n=10; M, n=8), mean age: 44±11 years (range: 20-60 years); CG: n=17 (F, n=10; M, n=7), mean age: 41±15 years (range: 20-65 years). IC: ability to walk (≥ 50 m) without assistance and MIRS grade 2–5
Missaoui et al. [21]	2010	France	Retrospective study	DM1	n=20 (F, n=7; M, n=13), mean age: 51 years (range: 32-69 years), IC: ability to walk unaided (≥ 10 m) and stand for 1 min

Abbreviations: MD, Muscular Dystrophy; DMD, Duchenne Muscular Dystrophy; M, Males; IC, Inclusion Criteria; ROM, Range of Motion; CG, Control Group; FSHD, Facioscapulohumeral dystrophy; F, Females; CSS, Clinical Severity Scale; RCT, Randomised Controlled Trial; SG, Study Group; CG, Control Group; DM1, Myotonic Dystrophy type 1; MIRS, Muscular Impairment Rating Scale; MRC, Medical Research Council; BMD, Becker Muscular Dystrophy; LGMD, Limb-girdle muscular dystrophy; CMD, Congenital Muscular Dystrophy; AFCSD, Ambulatory Functional Classification System for DMD; CBT, Cognitive Behavioural Therapy; ATG, Aerobic Training Group; DM2, Myotonic Dystrophy type 2; NSAA, North Star Ambulatory Assessment.

Supplementary file 6. Conservative non-pharmacological interventions included in the literature review and meta-analysis



*Multicomponent intervention included studies adopting intervention programmes consisting of three or more conservative non-pharmacological intervention types

Supplementary file 7. Characteristics of the interventions adopted in the included studies

Authors	Setting	Intervention	Intervention characteristics	Supervision	Adherence	Attrition	Adverse events
Orthotic devices							
Glanzman et al. (2011) [42]	Home-based	Serial casting	Below-knee serial casting. Individualised period of casting (range: 2 to 5 casts; mean: 3 casts). Casts applied with a comfortable dorsiflexed ankle position and were changed weekly, increasing dorsiflexion each time.	No	N.A.	N.A.	Foot pain (n=3). Focal redness (n=1).
Aprile et al. (2013) [43]	Home-based	AFO/FO	1 month use of customised ankle-foot/foot orthosis.	No	No information	None	None
Taktak et al. (1995) [44]	Inpatient, outpatient clinics, or schools	KAFO	2 months of daily use of the modular knee ankle foot orthosis combined with periodical use of the conventional knee ankle foot orthosis.	No	No information	n=2	None
Manual therapy							
Carroll et al. (2021) [18]	Outpatient clinics	Massage	10-minute calf massage (2 sessions), including effleurage (4 min), petrissage (3 min), and muscle stripping (3 min).	No	N.A.	None	None
Assistive technologies							
Heutinck et al. (2018) [30]	Home-based	Non-powered dynamic mobile arm support	SG: 20-week (5 times/week, 15 min per session) upper limb gravity-compensated 3D-training with suspension type arm support on a moveable frame. CG: usual care	Semi-supervised through home visits	Reported compliance was high.	SG: n=2 CG: n=4	Shoulder and thumb pain (n=1). Femur facture following a fall (unrelated to training) (n=1). Hospitalisation unrelated to training (n=1).
Vry et al. (2014) [45]	Outpatient clinics and home-based	WBVT	8-week WBVT (side-alternating) Week 1-4 (home-based), 5 days/week, 2 training sessions/day, (f=15-18 Hz). Week 5-8, (home-based), 5 days/week, 2 training/day, (f=18-24 Hz). Week 9-12: follow-up period (no training). Vibration platform exercises included mild squatting, gastrocnemius stretching and alternating weight shift.	Supervised and semi-supervised sessions via phone calls	No information	n=3	Muscle pain (1st day: n=6; 4 weeks: n=4; 8 weeks, n=1); muscle weakness (1st day, n=1; 4 weeks, n=4) and muscle cramps (4 weeks: n=1). Skin erythema or pruritus (1st day, n=1; 4 weeks, n=4). Talus facture (n=1)
Pegoraro et al. (2020) [47]	Inpatient setting	c-FES	c-FES for 15 days, 5 days/week, 30-minute daily session. Patients with contraindications to c-FES performed 6-weeks aerobic and strength training.	No	No information	None	None
Zupan et al. (1995) [16]	Home-based	FES	2/3-month tibialis anterior (right) electrical stimulation (1 hour-session, 2 times/day, f=8 Hz (8 participants) or 20 Hz (4 participants).	No	No information	None	None
Chisari et al. (2013) [46]	Home-based	NMES	Tibialis anterior electrical stimulation (phase on: 10 s; phase off: 10 s, f=20 Hz) for 15 days, two 60-minute daily sessions.	No	No information	None	None
Colson et al. (2010) [19]	Outpatient clinics	NMES	5-month program (35 Hz) for deltoid, trapezius transversalis, vastus lateralis, and vastus medialis. 5 sessions/week (20 min each), including electrical stimulation (2 min), 75 isometric contractions (1.5s rise, 6s steady tetanic stimulation, 1.5s fall; duty cycle: 56.25%), and 3-minute relaxation periods.	No	All participants completed all sessions.	None	Skin redness.
Kilinç et al. (2015) [22]	Outpatient clinics and home-based	HVPGS	Electrical stimulation group: 8-week training (deltoid and quadriceps femoris) (3 days/week), followed by an 8-week home-based program. Each muscle stimulated for 10 min at 50 Hz (phase on: 5s; phase off: 10s). Exercise group: 8-week strength exercises (deltoid and quadriceps femoris). 1-2 weeks: 25% of 1RM, 10 repetitions × 2 sets, 3 times/week. 2-4 weeks: 30% of 1RM, 10 repetitions × 3 sets, 3 times/week. 5-6 weeks: 35% of 1RM, 10 repetitions × 3 sets, 3 times/week. 7-8 weeks: 40% of 1RM 10 repetitions × 3 sets, 3 times/week.	Yes	No information	None	None
Ribot-Ciscar et al. (2015) [41]	Outpatient clinics	VPA	4-week training, one session (approx. 40 min - 1 hour) every 4 days (8 total sessions), targeting biceps brachialis, triceps brachialis and pectoralis major muscle (f=80 Hz). Each session: 6 vibratory blocks (e.g., shoulder abduction, shoulder elevation, elbow flexion and extension), 20-30 s rest in between.	No	All participants completed the intervention.	n=1	Pain (n=2)

Exercise interventions							
Authors	**Setting**	**Intervention**	**Intervention characteristics**	**Supervision**	**Adherence**	**Attrition**	**Adverse events**
Aerobic training							
Bulut et al. (2022) [38]	CG: home-based, SG: outpatient clinics and home-based	Aerobic training (cycle ergometer)	SG: 12-week exercise program combined with 12-week aerobic training (3 sessions/week). Each session lasted 40 min (5-minute warm up, 30-minute training and 5-minute cool-down). Training started at 60% HRmax, intensity reviewed every two weeks. CG: 12-week exercise program (3-5 times/week) including breathing exercises, stretching exercises, active-assisted, active and low-level resistance exercises, especially for lower limb muscles, and functional exercises (e.g., climbing and climbing stairs, taking steps).	CG: semi-supervised through biweekly phone calls. SG: supervised	Not available	SG: n=1 CG: n=2	None
Sherief et al. (2021) [32]	Outpatient clinics	Aerobic training (cycle ergometer vs treadmill)	Group A: 12-week exercise program (physiotherapy program combined with aerobic training on a cycle ergometer), 3 times/week. Each session lasted 20 min (5-minute warm up, 10 min training, 5-minute cool down). Resistance gradually increased on individual basis. Group B: 12-week exercise program (physiotherapy program combined with aerobic training on a treadmill), 3 times/week. Exercise training on treadmill lasted 20 min (5-minute warmup, 10 min training, 5-minute cool-down). Training practiced at 75% of over ground speed, no inclination. Physiotherapy program (group A and B): stretching exercises for biceps brachii, hamstrings and calf muscles (20 s each, performed 5 times); isometric muscle contractions for quadriceps, hamstrings, anterior tibial group, calf muscles, biceps and triceps muscles (contraction 5 s each, repeated 5 times); gait and balance training with obstacles.	No	Not available	None	None
Bankolé et al. (2016) [33]	Home-based	Aerobic training (stationary ergocycle)	SG: 6-month cycling training (3 sessions/week, each session lasting 35 min at 60% of MAP. CG: no intervention	Supervised and unsupervised sessions	>80%	SG: n=2	None
Mikhall et al. (2022) [55]	Laboratory	Aerobic training (cycle ergometer)	12-week cycling exercise program (3 sessions/week). Each training session included a 3-minute warmup (25 Watts) and a 2-minute cooldown (25 Watts). Training intensity: Week 1-2: 30 min at 65% V02max Week 3-4: 35 min at 65% V02max Week 5-6: 30 min at 70% V02max Week 7-8: 35 min at 70% V02max Week 9-10: 30 min at 75% V02max Week 11-12: 35 min at 75% V02max	Yes	60%	40% dropout rate	None
Sveen et al. (2008) [54]	Home-based	Aerobic training (cycle ergometer)	12-week training. Number of weekly sessions increased reaching 5 times/week (50 total sessions). Each session lasted 30 min, intensity: 65% of VO2max. After the 12 weeks, some participants continued to reach 1 year of training exercising 3 times/week.	Semi-supervised via weekly phone calls	12 weeks: 94% ± 2% (range: 75–100%). 1 year: 82% ± 3% (range: 74–88%)	None	None
Orngreen et al. (2005) [53]	Home-based	Aerobic training (cycle ergometer)	12-week training. Number of weekly sessions increased reaching 5 times/week (50 total sessions). Each session lasted 35 min, intensity: 65% of VO2max. Workload increased until exhaustion.	Semi-supervised via phone calls	92%	n=5	Worsening fatigue (n=1)
Aerobic training and/or cognitive behavioural therapy							
Okkersen et al. (2018) [23]	Outpatient clinics, home-based and community settings	CBT, standard care +/- aerobic training vs standard care	10-month of CBT plus standard care +/- optional graded exercises (SG) vs standard care alone (CG). CBT group: 10-14 sessions (each lasting between 15 and 75 min). Therapy focused on addressing reduced patient initiative, increasing physical activity, optimising social interaction, regulating sleep–wake patterns, coping with pain, and addressing beliefs about fatigue and living with muscular dystrophy. Graded exercises included moderate intensity aerobic exercises (e.g., walking, cycling or swimming) (between 120-170 min per week).	CG group was supervised	Not available	SG: n=8 at first F/U; n=6 at second F/U CG: n=5 at first F/U; n=1 at second F/U	50% of participants reported adverse events; of them, 226 (57%) were related to falls. 47 serious adverse events in 34 participants (13%).
Voet et al. (2014) [24]	Home-based and outpatient	Aerobic training (cycle ergometer) vs CBT vs usual	16-week aerobic training group vs 16-week CBT vs 16-week usual care. CBT: up to 6 CBT sessions. Session number decided on individual basis. Sessions targeted fatigue, cognition, pain, poor social support/interactions, and sleep disturbances. Each session lasted 50 min.	Supervised and unsupervised sessions	Insufficient adherence in 39% (n=11) of ATG and	n=1	Knee, neck, back, shoulder pain as well as saddle

	clinics	care	ATG: aerobic cycling training (30 min), 3 times/week, at 50-65% of HRR. Training included warm-up (5 min) and cool-down (3 min). Usual care: Occasional physiotherapy allowed (no fatigue-specific).		24% (n=6) of CBT group.		soreness (n=15).
Strength and aerobic training							
Kontou et al. (2020) [52]	Outpatient laboratory gym	Strength and aerobic training on stationary bicycle	4-week training, 2 times/week. Each session included 15-minute warm-up (10 min on a stationary bike at 25 Watts, 5-minute stretching), aerobic training on a stationary bicycle (15 min at 50% of MAP in the 1st week, 70% in the 3rd week), upper-limb and lower limb strength exercises (bench press, leg press, seated row, arm lateral raise, knee extension, leg curl, arm curl, elbow extension, calf raise, sit-ups and back extension). 2 sets of 12 repetitions at 50% of 10-RM (2-minute rest between sets).	Yes	Not available	None	None
Jensen et al. (2016) [51]	Outpatient clinics	Strength and aerobic training on an antigravity-treadmill	10-week training on an anti-gravity treadmill, 3 times/week, each session lasted 40 min. Strength exercises included closed-chain lower limb exercises (3 series per each exercise). Aerobic training: walk/run, jogging in place or high knee-lift at 70-80% of HR. Aerobic training was performed as interval training (1-2 min exercise, 1-minute rest). Training workload: 50% body weight support. Velocity individually set.	No	91% (range: 72–100%).	None	None
Berthelsen et al. (2014) [50]	Outpatient clinics	Strength and aerobic training on an antigravity-treadmill	Same protocol as the study above (Jensen et al. 20216).	Yes	91% (range: 72–100%).	None	None
Strength training							
Güneş Gencer et al. (2022) [34]	Home-based (conventional exercises) and outpatient clinics (trunk exercises)	Strength training	SG: 8-week conventional exercises (1 time/day) combined with trunk-oriented exercises (1 time/day). Daily sessions lasting 45 min, 5-10 repetitions. CG: 8-week conventional exercises (2 times/day). Daily sessions lasting 45 min, 5-10 repetitions. Conventional exercise program included stretching exercises, and active or active-assisted strength exercises targeting upper extremity, lower extremity, abdominal and back muscles. Trunk-oriented exercises included stretching exercises, stabilization exercises (active or active-assisted), arm exercises in fixed trunk position, trunk-oriented exercises (active or active-assisted), trunk mobilization (sitting and lying position), and functional upper limb reaching exercises.	SG group was supervised	Not available	None	None
Kenis-Coskun et al. (2022) [35]	Home-based	Strength training	SG: 8-week program, each session lased 30-40 min. 10 repetitions for each exercise. CG: 8-week home-based program, 3 times/week. 10 repetitions for each exercise. Both groups performed the same exercises: shoulder flexion, shoulder abduction, arm cross flexion exercise, elbow flexion- extension, wrist flexion- extension, hip flexion in sitting position, hip abduction in sitting position, ankle dorsiflexion in sitting position, Chin Tuck exercise, quadriceps strength exercise in sitting position, pectoral stretching exercise, trunk lateral stretching, posterior pelvic tilt exercise, bridge exercise, hip abductor strength exercise in side-lying position, tensor fascia latae stretching, hamstring stretching and Achilles tendon stretching.	SG group was supervised	97% (234/240) in SG and 83.3% (180/216) in CG.	SG: None CG: n=3	None
Maghbouli et al. (2021) [28]	Outpatient clinics	Strengthening training	SG: 6-week program using EMG-BFB, 2 times/week. Intensity: 50% of MVC. Exercise program included isometric strengthening exercises targeting hip flexors/extensors/adductors/abductors and knee flexors/extensors. CG: 6-week program, 2 times/week, each session lasted 30 min. Exercise program included isometric strengthening exercises targeting hip flexors/extensors/adductors/abductors and knee flexors/extensors.	CG group was supervised	60%	SG: n=7 CG: n=8	None
Alemdaroglu et al. (2015) [36]	CG: Home-based SG: Outpatient clinics	Strength training (arm ergometer)	SG: 8-week upper-limb training with arm ergometer (5 days/week). Each session lasted 40 min (5 min in passive mode (warm-up), 30 min in active mode and 5 min in passive mode (cooldown)). Intensity set at 50% of maximal difficulty level. CG: 8-weeks upper-limb range of motion training (e.g., shoulder flexion/extension/abduction, shoulder internal/external rotation, elbow flexion/extension and wrist flexion/extension), 3 times/week, each session lasted approx. 40 min. Each exercise repeated 5-10 times.	Yes	Not available	None	None
Aldehag et al. (2013) [39]	Home-based and outpatient clinics	Strength training (hand only)	12-week hand training exercises (3 times/week (one as a group session), each session lasted 1 hour), targeting mass wrist- and finger movements and isolated finger movements. Mass movements: Week 1-4: 1 set of 10 repetitions Week 5-8: 2 sets of 10 repetitions	Supervised and unsupervised sessions	Group A: <75%, n=2; ≥ 75%, n=9). Group B: <75%, n=10; ≥ 75%, n=4.	29% (group A, n=7; group B, n=2)	None

			Week 9-12: 3 sets of 10 repetitions Isolated finger movement: Week 1-4: 1 set of 3 repetitions Week 5-8: 2 sets of 3 repetitions Week 9-12: 3 sets of 3 repetitions				
Jansen et al. (2013) [29]	Home-based and school	Strength training	6-month assisted bicycle training (both arm and leg cycling), 5 days/week for 15 min. Cycling at a constant speed (65 revolutions/minute) and OMNI scale <6.	Assistance from parents or teachers	Adherence considered good overall.	SG: n=1	Knee/foot pain (n=3). Ankle trauma (n=1). Femur fracture (n=1).
Lindeman et al. (1995) [37]	Home-based	Strength training	SG: 24-week strength exercises (knee extension/flexion and hip extension/abduction), 30 min per session. Week 1-8: 3 sets of 25 repetitions with a load of 60% of 1RM. 1 minute rest between sets. Week 9-16: 3 sets of 15 repetitions with a load of 70% of 1RM. Week 17-24: 1 set of 10 repetitions with a load of 80% of 1RM. CG: no intervention	No	Compliance was defined as good.	n=4	Back pain (n=1)
O'Dowd et al. (2022) [40]	Outpatient clinics	Strength training	12-week training program (2 times/week) including 5-minute warm up, 5-minute balance training, step-ups, freestanding or assisted squats, knee flexion and extension on a knee extension and leg curl machine and six strength exercises (specific to each participant) (e.g., hip flexion, hip extension, plantar flexion, dorsiflexion, hip abduction, hip adduction, hip internal rotation, or hip external rotation exercises). Week 1-3: 2 sets of 10 RM. Exercise velocity: 2 s concentric, 4 s eccentric, 1-min rest between sets. Week 4-1: 3 sets of 10 RM. Exercise velocity: 2 s concentric, 4 s eccentric, 1-min rest between sets.	Yes	Compliance rate: 97%	None	None
Lessard et al. (2021) [27]	Home-based	Strength training	10-week strength training (3 times/week) including sit to stand, squat with wall support and alternated lunges. 2-4 sets with 5-8 repetitions, each repetition lasted 6 s, 1-minute rest between sets and 2-minute rest between each exercise. Intensity: 13-15 on Borg RPE scale.	Semi-supervised via weekly phone calls	96.7% (range: 90.0–100.0)	n=1	Persistent low back pain (n=1)
Roussel et al. (2020) [26]	Outpatient clinics	Strength training	12-week strength training (2 times/week, 21 sessions in total). Session included: 5-minute low-moderate intensity cycling, 3 series of 6-8 RM of five exercises (leg extension, leg press, hip abduction, squat and plantar flexion) (3-minute rest between exercises).	Yes	97%.	None	None
Bostock et al. (2019) [25]	Outpatient clinics	Strength training	12-week training including 2 sessions/week (24 total sessions). Each session included 5-minute warm up on a seated cross-trainer, cycle ergometer or rowing machine, 5-10 min of balance training using exergames, lower limb strength exercises with exercise machines and free weights. 2 sets of 10 RM (3 sets after third week). 1 minute rest between sets. Exercises velocity: 2 s concentric, 4 s eccentric.	Yes	13 participants completed all sessions.	n=2	Falls (n=1)
Tollbäck et al. (1999) [49]	Outpatient clinics	Strength training	12-week strength training (knee extensors) (3 times/week). Week 1: 3 sets of 8 repetitions with a load of 60% of 1RM. Week 2: 3 sets of 8 repetitions with a load of 70% of 1RM. Week 3-12: 3 sets of 8 repetitions with a load of 80% of 1RM. Each repetition lasted 9 s (concentric, isometric and eccentric phases, each lasting 3 s).	Yes	76% (range 69-85%) (based on 6 participants)	n=3	Knee pain. Increasing discomfort (n=1).
Hydrotherapy							
Hind et al. (2017) [17]	Swimming pool	Hydrotherapy vs land-based exercises	SG: 6-month hydrotherapy (2 times/week, each session lasting 30 min) combined with land-based exercises (4 days/week). CG: 6-month land-based exercise training, 6 days/week Hydrotherapy: upper and lower limb stretching exercises (e.g., hip flexors/extensors, hip abductors, knee extensors, ankle plantar flexors/dorsiflexors, wrist and finger flexors, neck flexors), aerobic exercises including walking, swimming, ball activities, functional activities (e.g., sit to stand, jumping, hopping) and breathing exercises. Land-based exercises: upper and lower limb stretching exercises (e.g., elbow extension, forearm supination, wrist/thumb/finger stretches, hip extension, iliotibial stretch, knee extension, ankle dorsiflexion, trunk and neck stretch in side flexion, trunk and neck stretches in rotation) as well as upper- and lower-limb strength exercises (e.g., shoulder abduction, shoulder flexion/extension, elbow extension, wrist and finger extension, hip extension/abduction, knee extension, trunk side flexion,	Yes	SG: 30-57% CG: 30-57%	CG: n=3	15 mild adverse events, including muscle soreness, falls related, chest infection and sleep hypoventilation.

			trunk extension, ankle dorsiflexion/plantarflexion). Each exercise repeated 5 times, with the position held for 3 s.				
Balance training							
Hammarén et al. (2015) [48]	Outpatient clinics	Balance program	10-week group program (e.g., sitting activities, weight transfers in sitting/standing, step training and walking) (1-3 times/week, each session lasted 60 min). Training also included lower limb stretching.	No	75% (average adherence)	n=2	None
Multicomponent intervention							
Kierkegaard et al. (2011) [20]	Outpatient clinics	Multicomponent intervention	SG: 14-week group training programme (2 times/week, each session lasted 60 min) including warm-up (9-10 min) flexibility (3-4 min), upper-limb and trunk strength (6-7 min), balance exercises (3-4 min), aerobic exercises (11-12 min at 60-80% of HRmax) and one brisk 30-minute walk/week. CG: no intervention	Yes	SG: ≥ 75% (n=11)	None	None
Missaoui et al. (2010) [21]	Outpatient clinics	Multicomponent intervention	6-week training (2/3 times/week, 2 hours each) (15 sessions in total) including static and dynamic balance exercises, knee strength training (10 repetitions, 5 sets), endurance training on a treadmill (20 min at 60% of HRR).	Yes	Compliance was reported to be low.	N.A.	None

Abbreviations: N.A., Not Applicable; AFO, Ankle-Foot Orthosis; FO, Foot Orthosis; SG, Study Group; CG, Control Group; WBVT, Whole-Body Vibration Therapy; c-FES, Functional Electrical Stimulation cycling; FES, Functional Electrical Stimulation; NMES, Neuromuscular Electrical Stimulation; HVPGS, High Voltage Pulsed Galvanic Stimulation; RM, Repetition Maximum; VPA, Vibratory Proprioceptive Assistance; HRmax, Maximum Heart Rate; MAP, Maximal Aerobic Power; VO2max, Maximal Oxygen Uptake; CBT, Cognitive Behavioural Therapy; F/U, Follow-Up; ATG, Aerobic Training Group; HRR, Heart Rate Reserve; HR, Heart Rate; EMG-BFB, Electromyography Biofeedback; MVC, Maximum Voluntary Contraction; RPE, Rating of Perceived Exertion.

Supplementary file 8. Effect sizes in the included conservative non-pharmacological interventions

Orthotic devices					
Intervention subtype	**Comparator**	**Sample size**	**Measure type**	**Outcome measures**	**ES (95% CI)**
Serial casting [42]	Before intervention vs after intervention	n=9	Body structure - PROM	Ankle dorsiflexion PROM (right knee extended)	2.28 (-1.75 to 6.3)
		n=6		Ankle dorsiflexion PROM (right knee flexed)	1.18 (-2.09 to 4.45)
		n=9		Ankle dorsiflexion PROM (left knee extended)	2.73 (-1.14 to 6.6)
		n=6		Ankle dorsiflexion PROM (left knee flexed)	1.88 (-1.78 to 5.54)
		n=9	Activities and participation - Mobility	10-m run time	-0.14 (-1.07 to 0.78)
		n=9		Timed Gower's sign	0.14 (-0.78 to 1.07)
		n=9		4SC	-0.06 (-0.99 to 0.86)
AFO/FO [43]	Before intervention vs after intervention	n=15	Activities and participation - Mobility	10mWT	0.82 (-0.07 to 1.71)
				2MWT	0.51 (-2.81 to 3.82)
				Rivermead Mobility Index	0.16 (-0.56 to 0.88)
			Activities and participation - Balance	BBS	0.51 (-0.5 to 1.51)
				Romberg index	0.75 (-25.28 to 26.77)
			Body function *(Patient-reported)*	NASS: Lneur	0.28 (-1.92 to 2.47)
			Pain	NASS: Lpain	0.26 (-1.17 to 1.69)
				VAS pain	0.09 (-0.63 to 0.81)
			Activities and participation - QoL	SF-36: physical functioning	0.11 (-0.92 to 1.13)
				SF-36: role physical	0.16 (-1.77 to -2.09)
				SF-36: bodily pain	-0.47 (-2.38 to 1.44)
				SF-36: general health	0.44 (-2.22 to 3.09)
				SF-36: vitality	0.49 (-2.16 to 3.15)
				SF-36: social functioning	0.55 (-3.02 to 4.11)
				SF-36: role emotional	0.27 (-2.24 to 2.78)
				SF-36: mental health	0.08 (-0.69 to 0.86)
				SF-36: physical component summary score	0.40 (-0.75 to 1.56)
				SF-36: mental component summary score	0.47 (-0.81 to 1.75)
KAFO[44]	Conventional KAFO vs modular KAFO	n=7	Body function	PCI walking (beats/min)	0.73 (-0.42 to 1.88)
			Activities and participation - Mobility	Walking speed	0.69 (-0.93 to 2.31)

Manual therapy					
Intervention subtype	**Comparator**	**Sample size**	**Measure type**	**Outcome measures**	**ES (95% CI)**
Calf massage [18]	Before intervention vs after intervention	n=20	Body structure - Muscle structure	Ankle dorsiflexion PROM (knee flexed)	0.51 (-0.34 to 1.37)
				Ankle dorsiflexion PROM (knee extended)	0.62 (-0.27 to 1.5)
				Knee extension PROM	-0.52 (-1.45 to 0.42)
			Activities and participation - Mobility	10m walk/run	0 (-0.62 to 0.62)
				Gait - speed	0.21 (-0.73 to 1.14)
				Gait - cadence	0.19 (-0.57 to 0.95)
				Gait - step length	0.15 (-0.49 to 0.79)
				Gait - base of support width	0.09 (-0.53 to 0.72)

Assistive technologies					
Intervention subtype	**Comparator**	**Sample size**	**Measure type**	**Outcome measures**	**ES (95% CI)**
Arm support [30]	Experimental treatment vs usual care treatment	SG:n=7; CG: n=9	Body function - AROM	Shoulder AROM	-0.07 (-3.96 to 3.82)
				Elbow AROM	0.78 (-10.47 to 12.03)
				Wrist AROM	0.11 (-2.07 to 2.29)
				Total upper limb AROM	0.15 (-10.99 to 11.29)
			Body function - Muscle strength	Left shoulder abduction (lbs)	-0.42 (-1.43 to 0.6)
				Right elbow flexion (lbs)	-0.17 (-1.58 to 1.24)
				Left elbow flexion (lbs)	-0.10 (-1.09 to 0.89)
				Right elbow extension (lbs)	0.38 (-0.71 to 1.47)
				Left elbow extension (lbs)	0.70 (-0.55 to 1.95)
				Shoulder maximal voluntary contraction (N)	0.17 (-4.3 to 4.65)
				Elbow maximal voluntary contraction (N)	0.02 (-0.98 to 1.02)
				Wrist maximal voluntary contraction (N)	0.30 (-3 to 3.61)
				Total upper limb maximal voluntary contraction (N)	0.25 (-7.02 to 7.53)
			Body function - Muscle endurance	A6MCT	-0.21 (-9.53 to 9.12)
			Activities and participation - Limbs function	PUL total score	0.11 (-1.03 to 1.24)
				PUL shoulder	-0.1 (-1.11 to 0.91)
				PUL elbow	0.22 (-0.97 to 1.41)
			Activities and participation - Functional activities	MFM D3 (%)	-0.11 (-1.12 to 0.9)
				Abilhand-plus	0.15 (-0.87 to 1.17)
			Activities and participation - QoL	Kidscreen-52	0.29 (-0.77 to 1.34)
WBVT [45]	Before intervention vs after intervention	n=12	Body function - AROM	Ankle dorsiflexion AROM (right)	0.65 (-0.74 to 2.04)
		n=12	Body function - Muscle strength	MRC leg sum score	0.30 (-1.35 to 1.95)
		n=12		Knee sum score (N)	0.41 (-1.31 to 2.14)
		n=11		Elbow flexion (N)	-0.07 (-0.95 to 0.82)
		n=12	Activities and participation - Mobility	6MWT	0.05 (-1.55 to 1.65)
		n=12		10mWT	0.10 (-0.71 to 0.90)
		n=12		4SC	0.20 (-0.61 to 1.02)
		n=12		Supine to stand test	-0.17 (-1.07 to 0.74)
FES	Before intervention vs	n=6	Body function - Muscle	Right tibialis anterior maximal torque (Nm)	1.19 (-0.3 to 2.67)

	after intervention [16]		strength		
	Before intervention vs after intervention [47]	n=8	Activities and participation - Mobility	6MWT	0.37 (-18.19 to 18.94)
				10mWT	0.30 (-1.02 to 1.62)
NMES	Before intervention vs after intervention [46]	n=6	Body function - Muscle strength	Total MRC score	0.63 (-0.52 to 1.78)
			Activities and participation - Mobility	10mWT	0.41 (-0.84 to 1.66)
				6MWT	0.32 (-7.9 to 8.53)
			Activities and participation - Balance	TUG	0.06 (-1.08 to 1.19)
	Before intervention vs after intervention [19]	n=9	Body function - Fatigue	VAS: Fatigue	0.52 (-0.41 to 1.46)
			Pain	VAS: Pain	**1.58 (0.61 to 2.55)**
			Activities and participation - Mobility	6MWT	0.66 (-8.57 to 9.89)
HVPGS[22]	Before intervention vs after intervention	n=13	Body function - Muscle strength	Right deltoid strength (N)	0.86 (-9.32 to 11.05)
				Left deltoid strength (N)	0.55 (-6.66 to 7.77)
				Right quadriceps femoris strength (N)	0.25 (-6.79 to 7.28)
				Left quadriceps femoris strength (N)	0.30 (-7.42 to 8.02)
			Body function - Muscle endurance	Right shoulder abduction (n. of repetitions in one minute)	0.31 (-1.51 to 2.12)
				Left shoulder abduction (n. of repetitions in one minute)	0.30 (-1.18 to 1.79)
				Right knee extension (n. of repetitions in one minute)	0.04 (-0.78 to 0.86)
				Left knee extension (n. of repetitions in one minute)	0.11 (-0.94 to 1.17)
			Activities and participation - Mobility	10mWT	0.10 (-0.71 to 0.90)
				Timed 8-stair climb	-0.05 (-0.85 to 0.76)
			Activities and participation – Functional activities	Dressing with a t-shirt (s)	-0.23 (-1.06 to 0.60)
				Lawton IADL test	0.01 (-0.79 to 0.82)
VPA[41]	Before intervention vs after intervention	n=8	Body function - Muscle strength	Shoulder abduction MVIC	**2.33 (1.32 to 3.34)**
			Activities and participation - QoL	SF-36: total score	1.56 (-2.38 to 5.49)
				SF-36: role emotional	1.58 (-3.03 to 6.19)
				Self-rated health state	2.33 (-4.32 to 8.99)

Exercise interventions					
Intervention subtype	**Comparator**	**Sample size**	**Impairment**	**Outcome measures**	**ES (95% CI)**
Aerobic training	Before intervention vs after intervention[55]	n=11	Body function	HR max	0.27 (-1.18 to 1.71)
	Before intervention vs after intervention (12 weeks)[54]	n=11		HR rest	0 (-0.84 to 0.84)
	Before intervention vs after intervention (12 months) [54]	n=11		HR rest	0.36 (-0.85 to 1.58)
	Before intervention vs after intervention (12 weeks)[54]	n=11		HR max	1.09 (-2.26 to 4.45)
	Before intervention vs after intervention (12 months)[54]	n=11		HR max	0.27 (-0.95 to 1.49)
	Before intervention vs after intervention[53]	n=12		HR	2.45 (-1.51 to 6.58)
	Before intervention vs after intervention[55]	n=11		PR interval	-0.28 (-3.04 to 2.48)
				QRS interval	-0.06 (-0.93 to 0.81)
	Before intervention vs after intervention [55]	n=11	Body structure - Body composition	Total lean mass (kg)	0.17 (-0.8 to 1.13)
				Total lean mass (kg)	0.16 (-0.8 to 1.12)
	Before intervention vs after intervention (12 weeks)[54]	n=10		Lean tissue mass - whole body (g)	-0.16 (-143.96 to 143.64)
	Before intervention vs after intervention (12 months)[54]			Lean tissue mass - whole body (g)	-1.84 (1349.6 to 1345.93)
	Before intervention vs after intervention [55]	n=11		Fat mass (kg)	0.04 (-0.8 to 0.89)
	Before intervention vs after intervention (12 weeks)[54]	n=10		Fat mass - whole body (g)	0.16 (-206.86 to 207.18)
	Before intervention vs after intervention (12 months)[54]			Fat mass - whole body (g)	0.38 (-415.2 to 415.96)
	Before intervention vs after intervention (12 weeks)[54]			Lean tissue mass - right leg (g)	-0.11 (-22.75 to 22.53)
	Before intervention vs after intervention (12 months)[54]			Lean tissue mass - right leg (g)	-1.08 (-200.35 to 198.19)
	Before intervention vs after intervention (12 weeks)[54]			Lean tissue mass - left leg (g)	-0.08 (-16.22 to 16.05)
	Before intervention vs after intervention (12 months)[54]			Lean tissue mass - left leg (g)	-1.22 (-211.33 to 208.9)
	Before intervention vs after intervention (12 weeks)[54]			Fat mass - right leg (g)	0.15 (-30.23 to 30.53)
	Before intervention vs after intervention (12 months)[54]			Fat mass - right leg (g)	0.52 (-86.57 to 87.6)
	Before intervention vs after intervention (12 weeks)[54]			Fat mass - left leg (g)	0.20 (-41.64 to 42.05)
	Before intervention vs after intervention (12 months)[54]			Fat mass - left leg (g)	0.57 (-99.22 to 100.36)
	Experimental treatment vs control treatment (no intervention) [33]	SG: n=8; CG: n=8	Body structure - Muscle structure	Whole muscle cross-sectional area	1.20 (-849.07 to 851.47)
	Experimental treatment vs control treatment [38]	SG: n=10; CG: n=9		Pennation angle - vastus lateralis (dominant side)	-0.07 (-0.97 to 0.84)
				Pennation angle - vastus lateralis (non-dominant side)	-0.62 (-1.96 to 0.71)
				Fascicle length - vastus lateralis (dominant side)	-0.06 (-0.97 to 0.84)
				Fascicle length - vastus lateralis (non-dominant side)	0.18 (-0.73 to 1.08)
				Muscle thickness - vastus lateralis (dominant side)	0.18 (-1.08 to 0.72)
				Muscle thickness - vastus lateralis (non-dominant side)	-0.44 (-1.35 to 0.46)
				Pennation angle - gastrocnemius (dominant side)	-0.29 (-1.31 to 0.73)
				Pennation angle - gastrocnemius (non-dominant side)	-0.11 (-1.03 to 0.81)
				Fascicle length - gastrocnemius (dominant side)	0.33 (-0.57 to 1.24)
				Fascicle length - gastrocnemius (non-dominant side)	0.34 (-0.56 to 1.25)
				Muscle thickness - gastrocnemius (dominant side)	-0.25 (-1.15 to 0.66)

			Muscle thickness - gastrocnemius (non-dominant side)	-0.25 (-1.15 to 0.66)
Before intervention vs after intervention [55]	n=11	Body structure - Bone structure	Bone mineral density (g/cm^2)	-0.3 (-1.14 to 0.53)
		Body function - Muscle strength	Knee extension (Nm)	0.02 (-0.87 to 0.9)
			Grip strength (kg)	-0.09 (-0.94 to 0.76)
			Pinch grip (kg)	-0.06 (-0.9 to 0.78)
Experimental intervention vs control intervention (no intervention) [33]	SG: n=8; CG: n=8		Maximal voluntary contraction at rest (Nm)	0.34 (-4.95 to 5.63)
			Voluntary activation at rest (%)	0.13 (-1.13 to 0.86)
Before intervention vs after intervention [54]	n=10		Hip flexion strength (N)	0 (-0.88 to 0.88)
			Hip extension strength (N)	0.19 (-1.08 to 1.47)
			Hip adduction strength (N)	0.22 (-1.06 to 1.5)
			Hip abduction strength (N)	0.09 (-0.84 to 1.02)
			Knee flexion strength (N)	0.75 (-3.07 to 4.57)
			Knee extension strength (N)	-0.89 (-6.24 to 4.45)
			Ankle dorsiflexion strength (N)	-1.67 (-7.31 to 3.98)
			Ankle plantarflexion strength (N)	2.85 (-4.33 to 10.03)
Experimental treatment vs control treatment [33]	SG: n=8; CG: n=8	Body function - Muscle endurance	Quadriceps endurance (n. of repetitions)	1.05 (-3.22 to 5.32)
		Activities and participation - Mobility	6MWT	0.55 (-21.65 to 22.74)
Experimental treatment vs control treatment [38]	SG: n=10; CG: n=9		6MWT	0.76 (-13.77 to 15.28)
Before intervention vs after intervention [55]	n=11		6MWT	0.67 (-13.24 to 14.59)
Experimental intervention (group A) vs control intervention (group B) [32]	SG: n=15; CG: n=15		6MWT	1.38 (-8.95 to 11.71)
Experimental treatment vs control treatment [38]	SG: n=10; CG: n=9	Activities and participation – Functional activities	MFM total score (%)	0.68 (-1.32 to 2.67)
			MFM-DI (%)	0.68 (-2.87 to 4.23)
			MFM-D2 (%)	0.42 (-0.68 to 1.52)
			MFM-D3 (%)	0.19 (-0.81 to 1.2)
Before intervention vs after intervention [55]	n=11	Activities and participation - Balance	TUG	0.73 (-0.16 to 1.6)
			5XSTS	1.11 (-0.3 to 2.24)
Experimental treatment vs control treatment [33]	SG: n=8; CG: n=8	Body function - Fatigue	FSS	1.14 (-4.15 to 6.43)
		Activities and participation - QoL	SF-36 total score	0.75 (-4.19 to 5.7)

Intervention subtype	Comparator	Sample size	Impairment	Outcome measures	ES (95% CI)
Aerobic training and/or CBT	Experimental intervention vs control intervention (usual care) [23]	SG: n=128; CG: n=127	Body function	Borg RPE score (end test)	0.16 (-0.08 to 0.41)
	Experimental intervention (aerobic training) vs control intervention (usual care) [24]	SG (aerobic training): n=20; CG (usual care): n=24	Body function - Muscle strength	Quadriceps MVIC	0.34 (-0.65 to 1.33)
	Experimental intervention (CBT) vs control intervention (usual care) [24]	SG (CBT): n=13; CG (usual care): n=24			-0.81 (-2.52 to 0.91)
	Experimental intervention (aerobic training) vs experimental intervention (CBT) [24]	SG (aerobic training): n=20; SG (CBT): n=13			-0.81 (-2.52 to 0.91)
	Experimental intervention vs control intervention (usual care) [23]	SG: n=128; CG: n=127	Activities and participation - Mobility	6MWT	0.23 (-2.47 to 2.93)
	Experimental intervention (aerobic training) vs control intervention (usual care) [24]	SG (aerobic training): n=20; CG (usual care): n=24			0.24 (-7.72 to 8.21)
	Experimental intervention (CBT) vs control intervention (usual care) [24]	SG (CBT): n=13; CG (usual care): n=24			-0.07 (-2.66 to 2.53)
	Experimental intervention (aerobic training) vs experimental intervention (CBT) [24]	SG (aerobic training): n=20; SG (CBT): n=13			-0.4 (-12.25 to 11.44)
	Experimental intervention vs control intervention (usual care) [23]	SG: n=128; CG: n=127	Body function - Fatigue	FDSS score	0.38 (-0.06 to 0.82)
				CIS-fatigue	0.45 (-0.005 to 0.89)
	Experimental intervention (aerobic training) vs control intervention (usual care) [24]	SG (aerobic training): n=20; CG (usual care): n=24		CIS-fatigue	0.41 (-0.46 to 1.27)
	Experimental intervention (CBT) vs control intervention (usual care) [24]	SG (CBT): n=13; CG (usual care): n=24			2.35 (-2.03 to 6.74)
	Experimental intervention (aerobic training) vs experimental intervention (CBT) [24]	SG (aerobic training): n=20; SG (CBT): n=13			1.65 (-2.27 to 5.58)
	Experimental intervention (aerobic training) vs control intervention (usual care) [24]	SG (aerobic training): n=20; CG (usual care): n=24		CIS-activity	-0.71 (-1.57 to 0.16)
	Experimental intervention (CBT) vs control intervention (usual care) [24]	SG (CBT): n=13; CG (usual care): n=24			0.48 (-0.33 to 1.29)
	Experimental intervention (aerobic training) vs experimental intervention (CBT) [24]	SG (aerobic training): n=20; SG (CBT): n=13			1.2 (-0.19 to 2.60)
	Experimental intervention vs control intervention (usual care) [23]	SG: n=128; CG: n=127	Activities and participation - QoL	INQOL quality of life	0.18 (-0.43 to 0.79)
				DM1-ActivC	0.27 (-0.22 to 0.77)
				MDHI score	0.17 (-0.19 to 0.53)
				BDI-FS score	-0.05 (-0.30 to 0.19)
				AES-c score	0.26 (-0.06 to 0.59)
	Experimental intervention (aerobic training) vs control intervention (usual care) [24]	SG (aerobic training): n=20; CG (usual care): n=24		NHP-sleep	0.88 (-3.10 to 4.87)
	Experimental intervention (CBT) vs control intervention (usual care) [24]	SG (CBT): n=13; CG (usual care): n=24			1.31 (-4.46 to 7.07)
	Experimental intervention (aerobic training) vs experimental intervention (CBT) [24]	SG (aerobic training): n=20; SG (CBT): n=13			0.32 (-1.35 to 1.99)
	Experimental intervention (aerobic training) vs control intervention (usual care) [24]	SG (aerobic training): n=20; CG (usual care): n=24		SIP68-sb	0.44 (-10.65 to 11.53)
	Experimental intervention (CBT) vs control intervention (usual care) [24]	SG (CBT): n=13; CG (usual care): n=24			0.12 (-2.91 to 3.16)
	Experimental intervention (aerobic training) vs experimental intervention (CBT) [24]	SG (aerobic training): n=20; SG (CBT): n=13			-0.3 (-9.97 to 9.38)
	Experimental intervention (aerobic training) vs control intervention (usual	SG (aerobic training): n=20;	Pain	VAS: pain	0.12 (-0.60 to 0.85)

	care) [24]	CG (usual care): n=24			
	Experimental intervention (CBT) vs control intervention (usual care) [24]	SG (CBT): n=13; CG (usual care): n=24			0.42 (-1.42 to 2.25)
	Experimental intervention (aerobic training) vs experimental intervention (CBT) [24]	SG (aerobic training): n=20; SG (CBT): n=13			0.31 (-1.19 to 1.81)
Strength training	Before intervention vs after intervention [49]	n=7	Body structure - Muscle structure	Cross-sectional area (mm^2)	0.11 (-23.62 to 23.83)
	Experimental intervention vs control intervention [29]	SG: n=15; CG: n=13	Body structure - PROM	Knee extension PROM	-0.39 (-4.23 to 3.45)
		SG: n=15; CG: n=13		Ankle dorsiflexion PROM	-0.22 (-1.89 to 1.44)
		SG: n=15; CG: n=13		Elbow extension PROM	-0.35 (-2.42 to 1.73)
	Experimental intervention vs control intervention [36]	SG: n=12; CG: n=12	Body function - Muscle strength *(upper limb)*	Right total upper limb strength (mean strength)	-0.06 (-0.86 to 0.74)
				Left total upper limb strength (mean strength)	-0.07 (-0.87 to 0.73)
	Experimental intervention vs control intervention [29]	SG: n=12; CG: n=14		MRC sum score: upper limb	0.15 (-0.63 to 0.93)
	Experimental intervention vs control intervention [35]	SG: n=10; SG: n=9		Neck flexion (kg)	-0.08 (-0.98 to 0.82)
				Neck extension (kg)	0.35 (-0.55 to 1.26)
				Right shoulder abduction (kg)	0.65 (-0.28 to 1.57)
				Left shoulder abduction (kg)	0.63 (-0.29 to 1.55)
	Experimental intervention vs control intervention [36]	SG: n=12; CG: n=12		Right shoulder girdle muscle strength (mean strength)	0.22 (-0.59 to 1.02)
				Left shoulder girdle muscle strength (mean strength)	0.18 (-0.63 to 0.97)
				Right scapulothoracic region (mean strength)	-0.06 (-0.86 to 0.74)
				Left scapulothoracic region (mean strength)	-0.07 (-0.88 to 0.73)
				Right upper limb muscles (mean strength)	-0.02 (-0.82 to 0.78)
				Left upper limb muscles (mean strength)	-0.01 (-0.81 to 0.79)
	Experimental intervention vs control intervention [35]	SG: n=10; SG: n=9		Right elbow flexion (kg)	-0.38 (-1.31 to 0.53)
				Left elbow flexion (kg)	0.16 (-0.74 to 1.07)
				Right elbow extension (kg)	-0.16 (-1.06 to 0.75)
				Left elbow extension (kg)	0.05 (-0.85 to 0.95)
	Experimental intervention vs control intervention [36]	SG: n=12; CG: n=12		Right forearm muscles (mean strength)	0 (-0.8 to 0.80)
				Left forearm muscles (mean strength)	-0.28 (-1.09 to 0.52)
	Experimental intervention vs control intervention [35]	SG: n=10; SG: n=9		Right wrist flexion (kg)	-0.06 (-0.96 to 0.84)
				Left wrist flexion (kg)	-0.16 (-1.06 to 0.74)
	Experimental intervention vs control intervention (no intervention) [39]	SG: n=18; CG: n=17		Isometric wrist flexion (N)	-0.05 (-0.86 to 0.76)
	Experimental intervention vs control intervention [35]	SG: n=10; SG: n=9		Right wrist extension (kg)	-0.37 (-1.27 to 0.53)
				Left wrist extension (kg)	-0.74 (-1.66 to 0.18)
	Experimental intervention vs control intervention (no intervention) [39]	SG: n=18; CG: n=17		Isometric wrist extension (N)	0.03 (-0.78 to 0.84)
				Hand grip (N)	0.03 (-0.94 to 0.99)
				Pinch grip (N)	0.1 (-0.71 to 0.90)
	Experimental intervention vs control intervention [29]	SG: n=12; CG: n=14	Body function - Muscle strength *(lower limb)*	MRC sum score: lower limb	0.34 (-0.51 to 1.18)
	Experimental intervention vs control intervention [35]	SG: n=10; SG: n=9		Right hip flexion (kg)	-0.48 (-1.40 to 0.45)
				Left hip flexion (kg)	0.14 (-0.76 to 1.04)
	Before intervention vs after intervention [27]	n=15		Maximal isometric hip flexion strength (Nm)	0.38 (-2.35 to 3.10)
	Experimental intervention vs control intervention [28]	SG: n=20; CG: n=20		Hip flexion (Nm)	0.22 (-0.42 to 0.85)
				Hip extension (Nm)	-0.27 (-0.91 to 0.37)
	Before intervention vs after intervention [27]	n=15		Maximal isometric hip extensors strength (Nm)	0.13 (-2.16 to 2.42)
	Experimental intervention vs control intervention [28]	SG: n=20; CG: n=20		Hip adduction strength (Nm)	-0.23 (-0.86 to 0.40)
	Before intervention vs after intervention [28]	n=11		Hip abduction (1RM)	1.3 (-20.16 to 22.77)
	Experimental intervention vs control intervention [35]	SG: n=10; SG: n=9		Left hip abduction (kg)	-0.14 (-1.04 to 0.76)
				Right hip abduction (kg)	-0.06 (-0.96 to 0.84)

Experimental intervention vs control intervention [28]	SG: n=20; CG: n=20		Hip abduction (Nm)	0.32 (-0.33 to 0.96)
Before intervention vs after intervention [27]	n=15		Maximal isometric hip abduction strength (Nm)	0.64 (-2.89 to 4.18)
			Maximal isometric knee flexion strength (Nm)	0.96 (-3.39 to 5.32)
Experimental intervention vs control intervention [35]	SG: n=10; SG: n=9		Right knee flexion (kg)	0.05 (-0.85 to 0.95)
			Left knee flexion (kg)	0.29 (-0.62 to 1.19)
Before intervention vs after intervention [25]	n=17		Knee flexion maximal voluntary contraction torque (Nm)	0.14 (-1.21 to 1.48)
Experimental intervention vs control intervention [28]	SG: n=20; CG: n=20		Knee flexion (Nm)	0.44 (-0.21 to 1.08)
Experimental intervention vs control intervention (no intervention) [37]	SG: n=15; CG: n=15		Isokinetic knee torque flexion (Nm)	0.21 (-0.97 to 1.38)
Experimental intervention vs control intervention [35]	SG: n=10; SG: n=9		Right knee extension (kg)	0.56 (-0.97 to 1.39)
			Left knee extension (kg)	0.18 (-0.72 to 1.09)
Before intervention vs after intervention [27]	n=15		Maximal isometric knee extension strength (Nm)	-0.18 (-2.37 to 2.02)
Before intervention vs after intervention [26]	n=11		Maximal isometric knee extension strength (Nm)	2.31 (-4.22 to 8.83)
Before intervention vs after intervention [25]	n=17		Knee extension maximal voluntary contraction torque (Nm)	0.06 (-1.37 to 1.49)
Experimental intervention vs control intervention (no intervention) [37]	SG: n=15; CG: n=15		Isokinetic knee torque extension (Nm)	0.11 (-1.11 to 1.33)
Experimental intervention vs control intervention [28]	SG: n=20; CG: n=20		Knee extension strength (Nm)	-0.05 (-0.67 to 0.56)
Experimental intervention vs control intervention [35]	SG: n=10; SG: n=9		Right ankle dorsiflexion (kg)	0.55 (-0.37 to 1.46)
			Left ankle dorsiflexion (kg)	0.68 (-0.24 to 1.60)
Before intervention vs after intervention [27]	n=15		Maximal isometric ankle dorsiflexion strength (Nm)	0 (-0.71 to 0.72)
Experimental intervention vs control intervention [35]	SG: n=10; SG: n=9		Right ankle plantarflexion (kg)	0.44 (-0.47 to 1.35)
			Left ankle plantarflexion (kg)	0.19 (-0.71 to 1.09)
Before intervention vs after intervention [26]	n=11		Leg extension (1 RM)	1.33 (-13.32 to 15.98)
			Leg press (1RM)	1.66 (-69.41 to 72.73)
			Squat (1RM)	2.52 (-73.39 to 78.44)
Experimental intervention vs control intervention [29]	SG: n=16; CG: n=13	Body function - Muscle endurance	A6MCT: legs	0.32 (-13.36 to 14.00)
	SG: n=16; CG: n=12		A6MCT: arms	0.18 (-6.62 to 6.98)
Experimental intervention vs control intervention [34]	SG: n=13; CG: n=13	Activities and participation – Limbs function	PUL total	1.12 (-0.02 to 2.26)
			PUL shoulder	0.6 (-0.17 to 1.37)
			PUL middle	0.34 (-0.47 to 1.16)
			PUL distal	**0.87 (0.04 to 1.69)**
Experimental intervention vs control intervention [36]	SG: n=12; CG: n=12		Timed T-shirt donning	0.24 (-0.83 to 1.32)
			Timed T-shirt removing	0.19 (-0.87 to 1.25)
Experimental intervention vs control intervention [36]	SG: n=12; CG: n=12		Upper limb unilateral placing (s)	0.09 (-0.93 to 1.11)
			Upper limb bilateral turning (s)	0.14 (-1.95 to 2.23)
Experimental intervention vs control intervention [29]	SG: n=16; CG: n=13		9HPT	0.07 (-0.67 to 0.81)
Experimental intervention vs control intervention (no intervention) [39]	SG: n=18; CG: n=17		N. of pegs placed on the Pegboard	-0.50 (-1.2 to 0.20)
Before intervention vs after intervention [27]	n=15		LEFS	0.68 (-1.46 to 2.83)
Before intervention vs after intervention [26]	n=11		LEFS	0.22 (-1.02 to 1.46)
Before intervention vs after intervention [29]	SG: n=17; CG: n=13	Activities and participation - Functional activities	Timed rise from floor	0.9 (-4.25 to 6.05)
Experimental intervention vs control intervention [36]	SG: n=12; CG: n=12		Supine to stand test	0.53 (-1.24 to 2.30)
Experimental intervention vs control intervention [35]	SG: n=10; SG: n=9		NSAA	-0.18 (-1.26 to 0.89)
Experimental intervention vs control intervention [36]	SG: n=12; CG: n=12		NSAA	0.12 (-0.74 to 0.97)
Experimental intervention vs control intervention [35]	SG: n=10; SG: n=9		QMFT score	-0.18 (-1.45 to 1.08)
Before intervention vs after intervention [29]	SG: n=17; CG: n=13		MFM-total (%)	0.46 (-1.49 to 2.42)
			MFM-D1 (%)	0.37 (-2.26 to 2.99)
			MFM-D2 (%)	0.3 (-1.03 to 1.62)
			MFM-D3 (%)	0.84 (-0.99 to 2.68)
Experimental intervention vs control intervention [35]	SG: n=10; SG: n=9	Activities and participation -	6MWT	0.06 (-3.30 to 3.42)
Before intervention vs after intervention [27]	n=15		6MWT	-0.09 (-2.72 to 2.54)

	Before intervention vs after intervention [26]	n=11	Mobility	10 MWT (comfortable speed)	0.43 (-0.41 to 1.26)
				10 MWT (maximal speed)	0.6 (-0.24 to 1.44)
	Before intervention vs after intervention [26]	n=15		10mWT (comfortable speed)	0.13 (-0.58 to 0.85)
				10mWT (maximal speed)	0 (-0.72 to 0.72)
	Before intervention vs after intervention [29]	SG: n=8; CG: n=8		10m run	-0.76 (-2.03 to 0.51)
	Before intervention vs after intervention [25,27]	n=17		Timed stair ascent	0.43 (-0.31 to 1.17)
				Timed stair descent	0.68 (-0.06 to 1.43)
	Before intervention vs after intervention [27]	n=15	Activities and participation - Balance	Mini BESTest	0.16 (-0.60 to 0.92)
				30CST	-0.06 (-0.79 to 0.66)
	Before intervention vs after intervention [26]	n=11		30CST	0.5 (-0.66 to 1.65)
	Before intervention vs after intervention [25]	n=17		STS	**0.83 (0.08 to 1.58)**
	Experimental intervention vs control intervention [34]	SG: n=13; CG: n=13		TCMS total	2.22 (-0.71 to 5.15)
				TCMS static sitting balance	**1.76 (0.82 to 2.71)**
				TCMS dynamic reaching	**2.29 (0.37 to 4.22)**
	Experimental intervention vs control intervention (no intervention) [39]	SG: n=18; CG: n=17	Activities and participation - QoL	AMPS (logits): motor skills	-0.50 (-1.17 to 0.17)
				AMPS (logits): process skills	-0.25 (-0.91 to 0.41)
	Experimental intervention vs control intervention [35]	SG: n=10; SG: n=9		Caregiver burden score	0.03 (-0.88 to 0.94)
	Before intervention vs after intervention [40]	n=17		SF-36: physical functioning	0.33 (-1.24 to 1.90)
				SF-36: role physical	0.51 (-2.88 to 3.90)
				SF-36: bodily pain	0.52 (-2.88 to 3.91)
				SF-36: general health	0.58 (-2.58 to 3.73)
				SF-36: vitality	0.66 (-2.49 to 3.82)
				SF-36: social functioning	0.53 (-3.33 to 4.39)
				SF-36: role emotional	0.50 (-3.13 to 4.12)
				SF-36: mental health	0.53 (-1.71 to 2.77)
				SF-36: physical component summary score	0.67 (-0.7 to 2.03)
				SF-36: mental component summary score	0.37 (-0.79 to 1.54)
				Physical self-worth: global (Physical Self-Perception Profile questionnaire)	0.67 (-0.16 to 1.49)
				Physical self-worth: sport competence (Physical Self-Perception Profile questionnaire)	0.33 (-0.38 to 1.04)
				Physical self-worth: physical condition (Physical Self-Perception Profile questionnaire)	**1 (0.17 to 1.82)**
				Physical self-worth: body attractiveness (Physical Self-Perception Profile questionnaire)	0.33 (-0.38 to 1.05)
				Physical self-worth: physical strength (Physical Self-Perception Profile questionnaire)	0 (-0.67 to 0.67)
	Before intervention vs after intervention [29]	SG: n=17; CG: n=13		PEDI: self-care	0.1 (-0.71 to 0.92)
				PEDI: mobility	-0.04 (-0.78 to 0.70)
	Experimental intervention vs control intervention (no intervention) [39]	SG: n=18; CG: n=17		COPM: performance	-0.14 (-0.81 to 0.52)
				COPM: satisfaction	0.08 (-0.58 to 0.74)
Strength and aerobic training	Before intervention vs after intervention [52]	n=10	Body function	Resting diastolic BP	1.29 (-2.35 to 4.93)
				Resting systolic BP	1.36 (-5.66 to 8.38)
				Post-testing diastolic BP	1.06 (-1.71 to 3.84)
				Post-testing systolic BP	1.40 (-4.86 to 7.66)
			Body structure - Body composition	Body fat (%)	0.37 (-0.76 to 1.49)
				Total LBM (kg)	0.25 (-0.76 to 1.26)

				LBM: arms (kg)	0.43 (-0.46 to 1.31)
				LBM: legs (kg)	0.29 (-0.61 to 1.18)
				LBM: trunk (kg)	0.14 (-0.75 to 1.03)
				Total BMD (g cm^{-2})	0.59 (-0.28 to 1.47)
				BMD: legs (g cm^{-2})	0.30 (-0.57 to 1.18)
				BMD: arms (g cm^{-2})	0.44 (-0.43 to 1.32)
				BMD: trunk (g cm^{-2})	0.66 (-0.22 to 1.53)
				BMD: femur (g cm^{-2})	0.40 (-0.48 to 1.28)
				BMD: femoral neck (g cm^{-2})	0.65 (-0.23 to 1.52)
			Body function - Muscle strength	Hand grip (kg)	0.22 (-0.91 to 1.36)
			Activities and participation - Mobility	6MWT	0.27 (-9.41 to 9.95)
			Activities and participation - Balance	5XSTS	0.83 (-2.09 to 3.76)
				TUG	0.47 (-0.93 to 1.86)
			Activities and participation - QoL	SF-36: general health	0.72 (-3.09 to 4.54)
				SF-36: bodily pain	-0.13 (-1.91 to 1.65)
				SF-36: social functioning	0.09 (-1.08 to 1.26)
				SF-36: role physical	0.42 (-2.75 to 3.58)
				SF-36: role emotional	0.23 (-1.42 to 1.88)
				SF-36: mental health	-0.22 (-2.47 to 2.04)
				SF-36: vitality	-0.09 (-1.20 to 1.02)
				SF-36: physical functioning	0.61 (-3.67 to 4.88)
	Before intervention vs after intervention [50]	n=6	Body function	HR (during submaximal test)	1.76 (-4.35 to 7.87)
	Before intervention vs after intervention [51]	n=8	Body function - Muscle strength	Isometric knee extension (N)	-0.22 (-2.52 to 2.08)
				Isometric knee flexion (N)	-0.31 (-3.91 to 3.29)
				Squat series performance (%BW/leg)	2.67 (-0.27 to 5.61)
				Calf raise series performance (%BW/leg)	1.90 (-4.76 to 8.55)
				Lunges performance	4.00 (-0.27 to 8.27)
			Activities and participation - Mobility	Walking distance (m/session)	1.60 (-67.01 to 70.21)
	Before intervention vs after intervention [50]	n=6		6MWT	0.65 (-13.4 to 14.69)
			Activities and participation - Balance	Dynamic postural balance test (s)	1.05 (-0.72 to 2.81)
Hydrotherapy	Before intervention vs after intervention [17]	n=8	Activities and participation - Mobility	6MWT	-0.27 (-7.96 to 7.41)
				NSAA	-0.40 (-1.79 to 0.99)
			Activities and participation - QoL	ACTIVLIM patient score	-0.50 (-2.06 to 1.06)
				ACTIVLIM patient measure	-0.65 (-1.66 to 0.37)
				CHU-9D	-0.57 (-1.55 to 0.41)
Balance training	Before intervention vs after intervention [48]	n=11	Body function - Muscle strength	Ankle dorsiflexion (N)	-0.61 (-3.67 to 2.46)
				Knee extension (N)	0 (-0.84 to 0.85)
			Activities and participation - Falls	Fall frequency	0.54 (-0.36 to 1.44)
			Activities and	10mWT	-0.18 (-1.03 to 0.67)

			participation - Mobility		
			Activities and participation - Balance	TUG	0.04 (-0.79 to 0.88)
Multicomponent intervention	Experimental intervention vs control intervention (no intervention) [20]	SG: n=18; CG: n=17	Body function	Borg RPE score	**3.83 (2.86 to 4.79)**
	Before intervention vs after intervention [21]	n=20	Body function - Muscle strength	Hamstrings isokinetic muscle strength (stronger side)	0.68 (-2.02 to 3.38)
				Hamstrings isometric muscle strength (weaker side)	0.52 (-1.76 to 2.79)
				Quadriceps isokinetic muscle strength quadriceps (stronger side)	0.08 (-0.82 to 0.98)
				Quadriceps isokinetic muscle strength (weaker side)	0.28 (-1.79 to 2.34)
	Experimental intervention vs control intervention (no intervention) [20]	SG: n=18; CG: n=17	Activities and participation - Mobility	6MWT	0.09 (-2.57 to 2.75)
	Before intervention vs after intervention [21]	n=20		Gait - slow speed	0.12 (-0.50 to 0.74)
				Gait - stride frequency (slow speed)	0.17 (-0.59 to 0.93)
				Gait - stride length (slow speed)	0 (-0.62 to 0.62)
				Gait - fast speed	**0.92 (0.26 to 1.57)**
				Gait - stride frequency (fast speed)	0.30 (-0.96 to 1.56)
				Gait - stride length (fast speed)	0 (-0.62 to 0.62)
			Activities and participation - Balance	FRT	0.49 (-0.69 to 1.67)
				BBS	0.40 (-0.63 to 1.43)
				TUG	0.42 (-0.41 to 1.25)
	Experimental intervention vs control intervention (no intervention) [20]	SG: n=18; CG: n=17		10XSTS	0.12 (-0.59 to 0.82)
				TUG	0.24 (-0.43 to 0.92)
			Activities and participation - QoL	SF- 36: physical functioning	0.72 (-1.27 to 2.70)
				SF- 36: role physical	-1.06 (-6.96 to 4.83)
				SF- 36: bodily pain	0.08 (-0.63 to 0.78)
				SF- 36: general health	1.20 (-1.46 to 3.86)
				SF- 36: vitality	0.65 (-0.69 to 1.99)
				SF- 36: social functioning	-1.94 (-6.44 to 2.56)
				SF- 36: role emotional	0.96 (-2.85 to 4.76)
				SF- 36: mental health	-1.33 (-6.07 to 3.39)
				ESS	-0.16 (-0.86 to 0.54)

Abbreviations: ES, Effect Size; CI, Confidence Interval; PROM, Passive Range of Motion; 4SC, Timed 4-stair climb; AFO, Ankle foot orthosis; FO, Foot orthosis; 10mWT, 10-meter walk test; 2MWT, 2 Minute Walk Test; BBS, Berg Balance Scale; NASS, North American Spine Society; Lneur, Lumbar spine neurogenic symptoms; Lpain, Lumbar spine pain/disability; VAS, Visual Analogue Scale; SF-36: 36-Item Short Form Health Survey; KAFO, Knee ankle foot orthosis; PCI, Physiological Cost Index; SG, Study Group; CG: Control Group; AROM, Active range of motion; A6MCT, Assisted 6 Minute Cycle Test; PUL, Performance of Upper Limb; MFM D3 (%), Motor function measure dimension 3; QoL, Quality of life; WBVT, Whole-Body Vibration Training; MRC, Medical Research Council; 6MWT, 6-minute walk test; FES, Functional Electrical Stimulation; NMES, Neuromuscular Electrical Stimulation; TUG, Timed Up and Go Test; HVPGS, High volt pulsed galvanic stimulator; IADL, Lawton Instrumental Activities of Daily Living; VPA, Vibratory Proprioceptive Assistance; MVIC, Maximal Voluntary Isometric contraction; SF-36, 36-Item Short Form Survey; HR, Heart Rate; 5XSTS, 5 times sit to stand; FSS, Fatigue Severity Scale; CBT, Cognitive Behavioural Therapy; RPE, Rating of Perceived Exertion; FDSS, Fatigue and daytime sleepiness scale; CIS-fatigue, Checklist Individual Strength-fatigue subscore; CIS-activity, Checklist Individual Strength-activity subscore; INQoL, Individualised Neuromuscular Quality of Life; DM1-ActivC, Myotonic Dystrophy type 1 Activity and participation scale; MDHI, Myotonic Dystrophy Health Index; BDI-FS, Beck Depression Inventory-Fast Screen; AES, Apathy Evaluation Scale; NHP-sleep, Nottingham Health Profile – sleep subscale; SIP68-sb, Sickness Impact Profile 68 – social behaviour subscale; 1RM, one repetition maximum; 9-HPT, 9-Hole Peg Test; LEFS, Lower Extremity Functional Scale; NSAA, North Star Ambulatory Assessment; 10MWT, 10 Minute Walk Test; 30CST, 30 Seconds Sit To Stand Test; STS, Sit to stand; TCMS, Trunk Control Measurement Scale; AMPS, Assessment of Motor and Process Skills; PEDI, Pediatric Evaluation of Disability Inventory; COPM, Canadian Occupational Performance Measure; BP, Blood Pressure; LBM, Lean Body Mass; BMD, Bone Mass Density; BW, Body Weight; CHU-9D, Child Health Utility 9D; FRT, Functional Reach Test; ESS, Epworth Sleepiness Scale.